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(54) **METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE**

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(57) **ABSTRACT**

The present invention relates to methods and compositions for monitoring, diagnosis, prognosis, and determination of treatment regimens in subjects suffering from or suspected of having a renal injury. In particular, the invention relates to using a one or more assays configured to detect a kidney injury marker selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 as diagnostic and prognostic biomarkers in renal injuries.

10 Claims, No Drawings

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METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE

The present invention is filed under 35 U.S.C. §371 as the U.S. national phase of International Application No. PCT/US2012/052298, filed Aug. 24, 2012, which designated the U.S. and claims priority to provisional U.S. patent application 61/528,000 filed Aug. 26, 2011, and to provisional U.S. patent application 61/528,003 filed Aug. 26, 2011, which is hereby incorporated in its entirety including all tables, figures, and claims.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Feb. 25, 2014, is named AST8104US_SeqListing.txt and is 51 kilobytes in size.

BACKGROUND OF THE INVENTION

The following discussion of the background of the invention is merely provided to aid the reader in understanding the invention and is not admitted to describe or constitute prior art to the present invention.

The kidney is responsible for water and solute excretion from the body. Its functions include maintenance of acid-base balance, regulation of electrolyte concentrations, control of blood volume, and regulation of blood pressure. As such, loss of kidney function through injury and/or disease

results in substantial morbidity and mortality. A detailed discussion of renal injuries is provided in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, which are hereby incorporated by reference in their entirety. Renal disease and/or injury may be acute or chronic. Acute and chronic kidney disease are described as follows (from Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, which are hereby incorporated by reference in their entirety): "Acute renal failure is worsening of renal function over hours to days, resulting in the retention of nitrogenous wastes (such as urea nitrogen) and creatinine in the blood. Retention of these substances is called azotemia. Chronic renal failure (chronic kidney disease) results from an abnormal loss of renal function over months to years".

Acute renal failure (ARF, also known as acute kidney injury, or AKI) is an abrupt (typically detected within about 48 hours to 1 week) reduction in glomerular filtration. This loss of filtration capacity results in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products that are normally excreted by the kidney, a reduction in urine output, or both. It is reported that ARF complicates about 5% of hospital admissions, 4-15% of cardiopulmonary bypass surgeries, and up to 30% of intensive care admissions. ARF may be categorized as prerenal, intrinsic renal, or postrenal in causation. Intrinsic renal disease can be further divided into glomerular, tubular, interstitial, and vascular abnormalities. Major causes of ARF are described in the following table, which is adapted from the Merck Manual, 17th ed., Chapter 222, and which is hereby incorporated by reference in their entirety:

Type Prerenal	Risk Factors
ECF volume depletion	Excessive diuresis, hemorrhage, GI losses, loss of intravascular fluid into the extravascular space (due to ascites, peritonitis, pancreatitis, or burns), loss of skin and mucus membranes, renal salt- and water-wasting states
Low cardiac output	Cardiomyopathy, MI, cardiac tamponade, pulmonary embolism, pulmonary hypertension, positive-pressure mechanical ventilation
Low systemic vascular resistance	Septic shock, liver failure, antihypertensive drugs
Increased renal vascular resistance	NSAIDs, cyclosporines, tacrolimus, hypercalcemia, anaphylaxis, anesthetics, renal artery obstruction, renal vein thrombosis, sepsis, hepatorenal syndrome
Decreased efferent arteriolar tone (leading to decreased GFR from reduced glomerular transcapillary pressure, especially in patients with bilateral renal artery stenosis)	ACE inhibitors or angiotensin II receptor blockers
Intrinsic Renal	
Acute tubular injury	Ischemia (prolonged or severe prerenal state): surgery, hemorrhage, arterial or venous obstruction; Toxins: NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, streptozotocin
Acute glomerulonephritis	ANCA-associated: Crescentic glomerulonephritis, polyarteritis nodosa, Wegener's granulomatosis; Anti-GBM glomerulonephritis: Goodpasture's syndrome; Immune-complex: Lupus glomerulonephritis, postinfectious glomerulonephritis, cryoglobulinemic glomerulonephritis
Acute tubulointerstitial nephritis	Drug reaction (eg, β-lactams, NSAIDs, sulfonamides, ciprofloxacin, thiazide diuretics, furosemide, phenytoin, allopurinol, pyelonephritis, papillary necrosis

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Type Prerenal	Risk Factors
Acute vascular nephropathy	Vasculitis, malignant hypertension, thrombotic microangiopathies, scleroderma, atheroembolism
Infiltrative diseases	Lymphoma, sarcoidosis, leukemia
Postrenal	
Tubular precipitation	Uric acid (tumor lysis), sulfonamides, triamterene, acyclovir, indinavir, methotrexate, ethylene glycol ingestion, myeloma protein, myoglobin
Ureteral obstruction	Intrinsic: Calculi, clots, sloughed renal tissue, fungus ball, edema, malignancy, congenital defects; Extrinsic: Malignancy, retroperitoneal fibrosis, ureteral trauma during surgery or high impact injury
Bladder obstruction	Mechanical: Benign prostatic hyperplasia, prostate cancer, bladder cancer, urethral strictures, phimosis, paraphimosis, urethral valves, obstructed indwelling urinary catheter; Neurogenic: Anticholinergic drugs, upper or lower motor neuron lesion

In the case of ischemic ARF, the course of the disease may be divided into four phases. During an initiation phase, which lasts hours to days, reduced perfusion of the kidney is evolving into injury. Glomerular ultrafiltration reduces, the flow of filtrate is reduced due to debris within the tubules, and back leakage of filtrate through injured epithelium occurs. Renal injury can be mediated during this phase by reperfusion of the kidney. Initiation is followed by an extension phase which is characterized by continued ischemic injury and inflammation and may involve endothelial damage and vascular congestion. During the maintenance phase, lasting from 1 to 2 weeks, renal cell injury occurs, and glomerular filtration and urine output reaches a minimum. A recovery phase can follow in which the renal epithelium is repaired and GFR gradually recovers. Despite this, the survival rate of subjects with ARF may be as low as about 60%.

Acute kidney injury caused by radiocontrast agents (also called contrast media) and other nephrotoxins such as cyclosporine, antibiotics including aminoglycosides and anticancer drugs such as cisplatin manifests over a period of days to about a week. Contrast induced nephropathy (CIN, which is AKI caused by radiocontrast agents) is thought to be caused by intrarenal vasoconstriction (leading to ischemic injury) and from the generation of reactive oxygen species that are directly toxic to renal tubular epithelial cells. CIN classically presents as an acute (onset within 24-48 h) but reversible (peak 3-5 days, resolution within 1 week) rise in blood urea nitrogen and serum creatinine.

A commonly reported criteria for defining and detecting AKI is an abrupt (typically within about 2-7 days or within a period of hospitalization) elevation of serum creatinine. Although the use of serum creatinine elevation to define and detect AKI is well established, the magnitude of the serum creatinine elevation and the time over which it is measured to define AKI varies considerably among publications. Traditionally, relatively large increases in serum creatinine such as 100%, 200%, an increase of at least 100% to a value over 2 mg/dL and other definitions were used to define AKI. However, the recent trend has been towards using smaller serum creatinine rises to define AKI. The relationship between serum creatinine rise, AKI and the associated health risks are reviewed in Praught and Shlipak, *Curr Opin Nephrol Hypertens* 14:265-270, 2005 and Chertow et al, *J Am Soc Nephrol* 16: 3365-3370, 2005, which, with the references listed therein, are hereby incorporated by reference in their entirety. As described in these publications, acute worsening renal function (AKI) and increased risk of death and other detrimental outcomes are now known to be associated with very small increases in serum creatinine. These increases may be determined as a relative (percent) value or a nominal value. Relative increases in serum creatinine as small as 20% from the pre-injury value have been reported to indicate acutely worsening renal function (AKI) and increased health risk, but the more commonly reported value to define AKI and increased health risk is a relative increase of at least 25%. Nominal increases as small as 0.3 mg/dL, 0.2 mg/dL or even 0.1 mg/dL have been reported to indicate worsening renal function and increased risk of death. Various time periods for the serum creatinine to rise to these threshold values have been used to define AKI, for example, ranging from 2 days, 3 days, 7 days, or a variable period defined as the time the patient is in the hospital or intensive care unit. These studies indicate there is not a particular threshold serum creatinine rise (or time period for the rise) for worsening renal function or AKI, but rather a continuous increase in risk with increasing magnitude of serum creatinine rise.

One study (Lassnigg et all, J Am Soc Nephrol 15:1597-1605, 2004, hereby incorporated by reference in its entirety) investigated both increases and decreases in serum creatinine. Patients with a mild fall in serum creatinine of −0.1 to −0.3 mg/dL following heart surgery had the lowest mortality rate. Patients with a larger fall in serum creatinine (more than or equal to −0.4 mg/dL) or any increase in serum creatinine had a larger mortality rate. These findings caused the authors to conclude that even very subtle changes in renal function (as detected by small creatinine changes within 48 hours of surgery) seriously effect patient's outcomes. In an effort to reach consensus on a unified classification system for using serum creatinine to define AKI in clinical trials and in clinical practice, Bellomo et al., *Crit Care.* 8(4):R204-12, 2004, which is hereby incorporated by reference in its entirety, proposes the following classifications for stratifying AKI patients:

"Risk": serum creatinine increased 1.5 fold from baseline OR urine production of <0.5 ml/kg body weight/hr for 6 hours;

"Injury": serum creatinine increased 2.0 fold from baseline OR urine production <0.5 ml/kg/hr for 12 h;

"Failure": serum creatinine increased 3.0 fold from baseline OR creatinine >355 μmol/l (with a rise of >44) or urine output below 0.3 ml/kg/hr for 24 h or anuria for at least 12 hours;

And included two clinical outcomes:

"Loss": persistent need for renal replacement therapy for more than four weeks.

"ESRD": end stage renal disease—the need for dialysis for more than 3 months.

These criteria are called the RIFLE criteria, which provide a useful clinical tool to classify renal status. As discussed in Kellum, *Crit. Care Med.* 36: S141-45, 2008 and Ricci et al., *Kidney Int.* 73, 538-546, 2008, each hereby incorporated by reference in its entirety, the RIFLE criteria provide a uniform definition of AKI which has been validated in numerous studies.

More recently, Mehta et al., *Crit. Care* 11:R31 (doi: 10.1186.cc5713), 2007, hereby incorporated by reference in its entirety, proposes the following similar classifications for stratifying AKI patients, which have been modified from RIFLE:

"Stage I": increase in serum creatinine of more than or equal to 0.3 mg/dL (≥26.4 μmol/L) or increase to more than or equal to 150% (1.5-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 6 hours;

"Stage II": increase in serum creatinine to more than 200% (>2-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 12 hours;

"Stage III": increase in serum creatinine to more than 300% (>3-fold) from baseline OR serum creatinine ≥354 μmol/L accompanied by an acute increase of at least 44 μmol/L OR urine output less than 0.3 mL/kg per hour for 24 hours or anuria for 12 hours.

The CIN Consensus Working Panel (McCollough et al, Rev Cardiovasc Med. 2006; 7(4):177-197, hereby incorporated by reference in its entirety) uses a serum creatinine rise of 25% to define Contrast induced nephropathy (which is a type of AKI). Although various groups propose slightly different criteria for using serum creatinine to detect AKI, the consensus is that small changes in serum creatinine, such as 0.3 mg/dL or 25%, are sufficient to detect AKI (worsening renal function) and that the magnitude of the serum creatinine change is an indicator of the severity of the AKI and mortality risk.

Although serial measurement of serum creatinine over a period of days is an accepted method of detecting and diagnosing AKI and is considered one of the most important tools to evaluate AKI patients, serum creatinine is generally regarded to have several limitations in the diagnosis, assessment and monitoring of AKI patients. The time period for serum creatinine to rise to values (e.g., a 0.3 mg/dL or 25% rise) considered diagnostic for AKI can be 48 hours or longer depending on the definition used. Since cellular injury in AKI can occur over a period of hours, serum creatinine elevations detected at 48 hours or longer can be a late indicator of injury, and relying on serum creatinine can thus delay diagnosis of AKI. Furthermore, serum creatinine is not a good indicator of the exact kidney status and treatment needs during the most acute phases of AKI when kidney function is changing rapidly. Some patients with AKI will recover fully, some will need dialysis (either short term or long term) and some will have other detrimental outcomes including death, major adverse cardiac events and chronic kidney disease. Because serum creatinine is a marker of filtration rate, it does not differentiate between the causes of AKI (pre-renal, intrinsic renal, post-renal obstruction, atheroembolic, etc) or the category or location of injury in intrinsic renal disease (for example, tubular, glomerular or interstitial in origin). Urine output is similarly limited, Knowing these things can be of vital importance in managing and treating patients with AKI.

These limitations underscore the need for better methods to detect and assess AKI, particularly in the early and subclinical stages, but also in later stages when recovery and repair of the kidney can occur. Furthermore, there is a need to better identify patients who are at risk of having an AKI.

BRIEF SUMMARY OF THE INVENTION

It is an object of the invention to provide methods and compositions for evaluating renal function in a subject. As described herein, measurement of one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 (each referred to herein as a "kidney injury marker") can be used for diagnosis, prognosis, risk stratification, staging, monitoring, categorizing and determination of further diagnosis and treatment regimens in subjects suffering or at risk of suffering from an injury to renal function, reduced renal function, and/or acute renal failure (also called acute kidney injury).

The kidney injury markers of the present invention may be used, individually or in panels comprising a plurality of kidney injury markers, for risk stratification (that is, to identify subjects at risk for a future injury to renal function, for future progression to reduced renal function, for future progression to ARF, for future improvement in renal function, etc.); for diagnosis of existing disease (that is, to identify subjects who have suffered an injury to renal function, who have progressed to reduced renal function, who have progressed to ARF, etc.); for monitoring for deterioration or improvement of renal function; and for predicting a future medical outcome, such as improved or worsening renal function, a decreased or increased mortality risk, a decreased or increased risk that a subject will require renal replacement therapy (i.e., hemodialysis, peritoneal dialysis, hemofiltration, and/or renal transplantation, a decreased or increased risk that a subject will recover from an injury to renal function, a decreased or increased risk that a subject will recover from ARF, a decreased or increased risk that a subject will progress to end stage renal disease, a decreased or increased risk that a subject will progress to chronic renal failure, a decreased or increased risk that a subject will suffer rejection of a transplanted kidney, etc.

In a first aspect, the present invention relates to methods for evaluating renal status in a subject. These methods comprise performing an assay method that is configured to detect one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase: Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 is/are then correlated to the renal status of the subject. This correlation to renal status may include correlating the assay result(s) to one or more of risk stratification, diagnosis, prognosis, staging, classifying and monitoring of the subject as described herein. Thus, the present invention utilizes one or more kidney injury markers of the present invention for the evaluation of renal injury.

In certain embodiments, the methods for evaluating renal status described herein are methods for risk stratification of the subject; that is, assigning a likelihood of one or more future changes in renal status to the subject. In these embodiments, the assay result(s) is/are correlated to one or more such future changes. The following are preferred risk stratification embodiments.

In preferred risk stratification embodiments, these methods comprise determining a subject's risk for a future injury to renal function, and the assay result(s) is/are correlated to a likelihood of such a future injury to renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

In other preferred risk stratification embodiments, these methods comprise determining a subject's risk for future reduced renal function, and the assay result(s) is/are correlated to a likelihood of such reduced renal function. For example, the measured concentrations may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future reduced renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of future reduced renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

In still other preferred risk stratification embodiments, these methods comprise determining a subject's likelihood for a future improvement in renal function, and the assay result(s) is/are correlated to a likelihood of such a future improvement in renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold. For a "negative going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold.

In yet other preferred risk stratification embodiments, these methods comprise determining a subject's risk for progression to ARF, and the result(s) is/are correlated to a likelihood of such progression to ARF. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

And in other preferred risk stratification embodiments, these methods comprise determining a subject's outcome risk, and the assay result(s) is/are correlated to a likelihood of the occurrence of a clinical outcome related to a renal injury suffered by the subject. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic kidney disease, etc., is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic kidney disease, etc., is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

In such risk stratification embodiments, preferably the likelihood or risk assigned is that an event of interest is more or less likely to occur within 180 days of the time at which the body fluid sample is obtained from the subject. In particularly preferred embodiments, the likelihood or risk assigned relates to an event of interest occurring within a shorter time period such as 18 months, 120 days, 90 days, 60 days, 45 days, 30 days, 21 days, 14 days, 7 days, 5 days, 96 hours, 72 hours, 48 hours, 36 hours, 24 hours, 12 hours, or less. A risk at 0 hours of the time at which the body fluid sample is obtained from the subject is equivalent to diagnosis of a current condition.

In preferred risk stratification embodiments, the subject is selected for risk stratification based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF. For example, a subject undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery; a subject having pre-existing congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, or sepsis; or a subject exposed to NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin are all preferred subjects for monitoring risks according to the methods described herein. This list is not meant to be limiting. By "pre-existence" in this context is meant that the risk factor exists at the time the body fluid sample is obtained from the subject. In particularly preferred embodiments, a subject is chosen for risk stratification based on an existing diagnosis of injury to renal function, reduced renal function, or ARF.

In other embodiments, the methods for evaluating renal status described herein are methods for diagnosing a renal injury in the subject; that is, assessing whether or not a subject has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay

result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 is/are correlated to the occurrence or nonoccurrence of a change in renal status. The following are preferred diagnostic embodiments.

In preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of such an injury. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

In other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing reduced renal function. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

In yet other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing ARF. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal replacement therapy, and the assay result(s) is/are correlated to a need for renal replacement therapy. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal transplantation, and the assay result (s0 is/are correlated to a need for renal transplantation. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal transplantation is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal transplantation is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an

increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

In still other embodiments, the methods for evaluating renal status described herein are methods for monitoring a renal injury in the subject; that is, assessing whether or not renal function is improving or worsening in a subject who has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 receptor is/are correlated to the occurrence or nonoccurrence of a change in renal status. The following are preferred monitoring embodiments.

In preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

In other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

In yet other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from acute renal failure, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

In other additional preferred monitoring embodiments, these methods comprise monitoring renal status in a subject at risk of an injury to renal function due to the pre-existence of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

In still other embodiments, the methods for evaluating renal status described herein are methods for classifying a renal injury in the subject; that is, determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage. In these embodiments, the assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 is/are correlated to a particular class and/or subclass. The following are preferred classification embodiments.

In preferred classification embodiments, these methods comprise determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage, and the assay result(s) is/are correlated to the injury classification for the subject. For example, the measured concentration may be compared to a threshold value, and when the measured concentration is above the threshold, a particular classification is assigned; alternatively, when the measured concentration is below the threshold, a different classification may be assigned to the subject.

A variety of methods may be used by the skilled artisan to arrive at a desired threshold value for use in these methods. For example, the threshold value may be determined from a population of normal subjects by selecting a concentration representing the 75th, 85th, 90th, 95th, or 99th percentile of a kidney injury marker measured in such normal subjects. Alternatively, the threshold value may be determined from a "diseased" population of subjects, e.g., those suffering from an injury or having a predisposition for an injury (e.g., progression to ARF or some other clinical

outcome such as death, dialysis, renal transplantation, etc.), by selecting a concentration representing the 75th, 85th, 90th, 95th, or 99th percentile of a kidney injury marker measured in such subjects. In another alternative, the threshold value may be determined from a prior measurement of a kidney injury marker in the same subject; that is, a temporal change in the level of a kidney injury marker in the subject may be used to assign risk to the subject.

The foregoing discussion is not meant to imply, however, that the kidney injury markers of the present invention must be compared to corresponding individual thresholds. Methods for combining assay results can comprise the use of multivariate logistical regression, log linear modeling, neural network analysis, n-of-m analysis, decision tree analysis, calculating ratios of markers, etc. This list is not meant to be limiting. In these methods, a composite result which is determined by combining individual markers may be treated as if it is itself a marker; that is, a threshold may be determined for the composite result as described herein for individual markers, and the composite result for an individual patient compared to this threshold.

The ability of a particular test to distinguish two populations can be established using ROC analysis. For example, ROC curves established from a "first" subpopulation which is predisposed to one or more future changes in renal status, and a "second" subpopulation which is not so predisposed can be used to calculate a ROC curve, and the area under the curve provides a measure of the quality of the test. Preferably, the tests described herein provide a ROC curve area greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95.

In certain aspects, the measured concentration of one or more kidney injury markers, or a composite of such markers, may be treated as continuous variables. For example, any particular concentration can be converted into a corresponding probability of a future reduction in renal function for the subject, the occurrence of an injury, a classification, etc. In yet another alternative, a threshold that can provide an acceptable level of specificity and sensitivity in separating a population of subjects into "bins" such as a "first" subpopulation (e.g., which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc.) and a "second" subpopulation which is not so predisposed. A threshold value is selected to separate this first and second population by one or more of the following measures of test accuracy:

an odds ratio greater than 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less;

a specificity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding sensitivity greater than 0.2, preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

a sensitivity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding specificity greater than 0.2, preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

at least about 75% sensitivity, combined with at least about 75% specificity;

a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least about 2, more preferably at least about 3, still more preferably at least about 5, and most preferably at least about 10; or

a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal to about 0.5, more preferably less than or equal to about 0.3, and most preferably less than or equal to about 0.1.

The term "about" in the context of any of the above measurements refers to +/−5% of a given measurement.

Multiple thresholds may also be used to assess renal status in a subject. For example, a "first" subpopulation which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc., and a "second" subpopulation which is not so predisposed can be combined into a single group. This group is then subdivided into three or more equal parts (known as tertiles, quartiles, quintiles, etc., depending on the number of subdivisions). An odds ratio is assigned to subjects based on which subdivision they fall into. If one considers a tertile, the lowest or highest tertile can be used as a reference for comparison of the other subdivisions. This reference subdivision is assigned an odds ratio of 1. The second tertile is assigned an odds ratio that is relative to that first tertile. That is, someone in the second tertile might be 3 times more likely to suffer one or more future changes in renal status in comparison to someone in the first tertile. The third tertile is also assigned an odds ratio that is relative to that first tertile.

In certain embodiments, the assay method is an immunoassay. Antibodies for use in such assays will specifically bind a full length kidney injury marker of interest, and may also bind one or more polypeptides that are "related" thereto, as that term is defined hereinafter. Numerous immunoassay formats are known to those of skill in the art. Preferred body fluid samples are selected from the group consisting of urine, blood, serum, saliva, tears, and plasma. In the case of those kidney injury markers which are membrane proteins as described hereinafter, preferred assays detect soluble forms thereof.

The foregoing method steps should not be interpreted to mean that the kidney injury marker assay result(s) is/are used in isolation in the methods described herein. Rather, additional variables or other clinical indicia may be included in the methods described herein. For example, a risk stratification, diagnostic, classification, monitoring, etc. method may combine the assay result(s) with one or more variables measured for the subject selected from the group consisting of demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (e.g., blood pressure, temperature, respiration rate), risk scores (APACHE score, PRE-DICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score, risk scores of Thakar et al. (J. Am. Soc. Nephrol. 16: 162-68, 2005), Mehran et al. (J. Am. Coll. Cardiol. 44: 1393-99, 2004), Wijeysundera et al. (JAMA 297: 1801-9, 2007), Goldstein and Chawla (Clin. J. Am. Soc. Nephrol. 5: 943-49, 2010), or Chawla et al. (Kidney Intl. 68: 2274-80, 2005)), a glomerular filtration rate, an

estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatinine ratio, a renal failure index calculated as urine sodium/(urine creatinine/plasma creatinine), a serum or plasma neutrophil gelatinase (NGAL) concentration, a urine NGAL concentration, a serum or plasma cystatin C concentration, a serum or plasma cardiac troponin concentration, a serum or plasma BNP concentration, a serum or plasma NTproBNP concentration, and a serum or plasma proBNP concentration. Other measures of renal function which may be combined with one or more kidney injury marker assay result(s) are described hereinafter and in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

When more than one marker is measured, the individual markers may be measured in samples obtained at the same time, or may be determined from samples obtained at different (e.g., an earlier or later) times. The individual markers may also be measured on the same or different body fluid samples. For example, one kidney injury marker may be measured in a serum or plasma sample and another kidney injury marker may be measured in a urine sample. In addition, assignment of a likelihood may combine an individual kidney injury marker assay result with temporal changes in one or more additional variables.

In various related aspects, the present invention also relates to devices and kits for performing the methods described herein. Suitable kits comprise reagents sufficient for performing an assay for at least one of the described kidney injury markers, together with instructions for performing the described threshold comparisons.

In certain embodiments, reagents for performing such assays are provided in an assay device, and such assay devices may be included in such a kit. Preferred reagents can comprise one or more solid phase antibodies, the solid phase antibody comprising antibody that detects the intended biomarker target(s) bound to a solid support. In the case of sandwich immunoassays, such reagents can also include one or more detectably labeled antibodies, the detectably labeled antibody comprising antibody that detects the intended biomarker target(s) bound to a detectable label. Additional optional elements that may be provided as part of an assay device are described hereinafter.

Detectable labels may include molecules that are themselves detectable (e.g., fluorescent moieties, electrochemical labels, ecl (electrochemical luminescence) labels, metal chelates, colloidal metal particles, etc.) as well as molecules that may be indirectly detected by production of a detectable reaction product (e.g., enzymes such as horseradish peroxidase, alkaline phosphatase, etc.) or through the use of a specific binding molecule which itself may be detectable (e.g., a labeled antibody that binds to the second antibody, biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, etc.).

Generation of a signal from the signal development element can be performed using various optical, acoustical, and electrochemical methods well known in the art. Examples of detection modes include fluorescence, radiochemical detection, reflectance, absorbance, amperometry, conductance, impedance, interferometry, ellipsometry, etc. In certain of these methods, the solid phase antibody is coupled to a transducer (e.g., a diffraction grating, electrochemical sensor, etc) for generation of a signal, while in others, a signal is generated by a transducer that is spatially separate from the solid phase antibody (e.g., a fluorometer that employs an excitation light source and an optical detector). This list is not meant to be limiting. Antibody-based biosensors may also be employed to determine the presence or amount of analytes that optionally eliminate the need for a labeled molecule.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to methods and compositions for diagnosis, differential diagnosis, risk stratification, monitoring, classifying and determination of treatment regimens in subjects suffering or at risk of suffering from injury to renal function, reduced renal function and/or acute renal failure through measurement of one or more kidney injury markers. In various embodiments, a measured concentration of one or more biomarkers selected from the group consisting of Heat shock 70 kDa protein 1, Alpha-1-antitrypsin Neutrophil elastase complex, Stromelysin-1:Metalloproteinase inhibitor 2 complex, 72 kDa type IV collagenase: Metalloproteinase inhibitor 2 complex, Insulin-like growth factor 1 receptor, Myeloid differentiation primary response protein MyD88, Neuronal cell adhesion molecule, and Tumor necrosis factor ligand superfamily member 10 or one or more markers related thereto, are correlated to the renal status of the subject.

For purposes of this document, the following definitions apply:

As used herein, an "injury to renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable reduction in a measure of renal function. Such an injury may be identified, for example, by a decrease in glomerular filtration rate or estimated GFR, a reduction in urine output, an increase in serum creatinine, an increase in serum cystatin C, a requirement for renal replacement therapy, etc "Improvement in Renal Function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable increase in a measure of renal function. Preferred methods for measuring and/or estimating GFR are described hereinafter.

As used herein, "reduced renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.1 mg/dL (≥8.8 μmol/L), a percentage increase in serum creatinine of greater than or equal to 20% (1.2-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour).

As used herein, "acute renal failure" or "ARF" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.3 mg/dl (≥26.4 μmol/l), a percentage increase in serum creatinine of greater than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for at least 6 hours). This term is synonymous with "acute kidney injury" or "AKI."

As used herein, the term "Heat shock 70 kDa protein 1" refers to one or more polypeptides present in a biological sample that are derived from the Heat shock 70 kDa protein 1 precursor (human precursor Swiss-Prot P08107 (SEQ ID NO: 1)).

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        10         20         30         40         50         60
MAKAAAIGID LGTTYSCVGV FQHGKVEIIA NDQGNRTTPS YVAFTDTERL IGDAAKNQVA

        70         80         90        100        110        120
LNPQNTVFDA KRLIGRKFGD PVVQSDMKHW PFQVINDGDK PKVQVSYKGE TKAFYPEEIS

       130        140        150        160        170        180
SMVLTKMKEI AEAYLGYPVT NAVITVPAYF NDSQRQATKD AGVIAGLNVL RIINEPTAAA

       190        200        210        220        230        240
IAYGLDRTGK GERNVLIFDL GGGTFDVSIL TIDDGIFEVK ATAGDTHLGG EDFDNRLVNH

       250        260        270        280        290        300
FVEEFKRKHK KDISQNKRAV RRLRTACERA KRTLSSSTQA SLEIDSLFEG IDFYTSITRA

       310        320        330        340        350        360
RFEELCSDLF RSTLEPVEKA LRDAKLDKAQ IHDLVLVGGS TRIPKVQKLL QDFFNGRDLN

       370        380        390        400        410        420
KSINPDEAVA YGAAVQAAIL MGDKSENVQD LLLLDVAPLS LGLETAGGVM TALIKRNSTI

       430        440        450        460        470        480
PTKQTQIFTT YSDNQPGVLI QVYEGERAMT KDNNLLGRFE LSGIPPAPRG VPQIEVTFDI

       490        500        510        520        530        540
DANGILNVTA TDKSTGKANK ITITNDKGRL SKEEIERMVQ EAEKYKAEDE VQRERVSAKN

       550        560        570        580        590        600
ALESYAFNMK SAVEDEGLKG KISEADKKKV LDKCQEVISW LDANTLAEKD EFEHKRKELE

       610        620        630        640
QVCNPIISGL YQGAGGPGPG GFGAQGPKGG SGSGPTIEEV D
```

The following domains have been identified in Heat shock 70 kDa protein 1:

Residues	Length	Domain ID
1	1	Initiator methionine
2-641	640	Heat shock 70 kDa protein 1

As used herein, the term "Stromelysin-1:Metalloproteinase inhibitor 2 complex" refers to a polypeptide complex present in a biological sample that comprises one or more polypeptides that are derived from the Stromelysin-1 precursor and one or more polypeptides that are derived from the Metalloproteinase inhibitor 2 precursor.

used herein, the term "72 kDa type IV collagenase: Metalloproteinase inhibitor 2 complex" refers to a polypeptide complex present in a biological sample that comprises one or more polypeptides that are derived from the 72 kDa type IV collagenase precursor and one or more polypeptides that are derived from the Metalloproteinase inhibitor 2 precursor.

The human Stromelysin-1 precursor has the following sequence (Swiss-Prot P08254 (SEQ ID NO: 2)):

```
        10         20         30         40         50         60
MKSLPILLLL CVAVCSAYPL DGAARGEDTS MNLVQKYLEN YYDLKKDVKQ FVRRKDSGPV

        70         80         90        100        110        120
VKKIREMQKF LGLEVTGKLD SDTLEVMRKP RCGVPDVGHF RTFPGIPKWR KTHLTYRIVN

       130        140        150        160        170        180
YTPDLPKDAV DSAVEKALKV WEEVTPLTFS RLYEGEADIM ISFAVREHGD FYPFDGPGNV

       190        200        210        220        230        240
LAHAYAPGPG INGDAHFDDD EQWTKDTTGT NLFLVAAHEI GHSLGLFHSA NTEALMYPLY

       250        260        270        280        290        300
HSLTDLTRFR LSQDDINGIQ SLYGPPPDSP ETPLVPTEPV PPEPGTPANC DPALSFDAVS

       310        320        330        340        350        360
TLRGEILIFK DRHFWRKSLR KLEPELHLIS SFWPSLPSGV DAAYEVTSKD LVFIFKGNQF

       370        380        390        400        410        420
WAIRGNEVRA GYPRGIHTLG FPPTVRKIDA AISDKEKNKT YFFVEDKYWR FDEKRNSMEP

       430        440        450        460        470
GFPKQIAEDF PGIDSKIDAV FEEFGFFYFF TGSSQLEFDP NAKKVTHTLK SNSWLNC
```

The following domains have been identified in Stromelysin-1:

Residues	Length	Domain ID
1-17	17	signal sequence
18-99	82	propeptide
100-477	378	Stromelysin-1

The human 72 kDa type IV collagenase precursor (Swiss-Prot P08253 (SEQ ID NO: 3)) has the following sequence:

```
        10         20         30         40         50         60
MEALMARGAL TGPLRALCLL GCLLSHAAAA PSPIIKFPGD VAPKTDKELA VQYLNTFYGC

        70         80         90        100        110        120
PKESCNLFVL KDTLKKMQKF FGLPQTGDLD QNTIETMRKP RCGNPDVANY NFFPRKPKWD

       130        140        150        160        170        180
KNQITYRIIG YTPDLDPETV DDAFARAFQV WSDVTPLRFS RIHDGEADIM INFGRWEHGD

       190        200        210        220        230        240
GYPFDGKDGL LAHAFAPGTG VGGDSHFDDD ELWTLGEGQV VRVKYGNADG EYCKFPFLFN

       250        260        270        280        290        300
GKEYNSCTDT GRSDGFLWCS TTYNFEKDGK YGFCPHEALF TMGGNAEGQP CKFPFRFQGT

       310        320        330        340        350        360
SYDSCTTEGR TDGYRWCGTT EDYDRDKKYG FCPETAMSTV GGNSEGAPCV FPFTFLGNKY

       370        380        390        400        410        420
ESCTSAGRSD GKMWCATTAN YDDDRKWGFC PDQGYSLFLV AAHEFGHAMG LEHSQDPGAL

       430        440        450        460        470        480
MAPIYTYTKN FRLSQDDIKG IQELYGASPD IDLGTGPTPT LGPVTPEICK QDIVFDGIAQ

       490        500        510        520        530        540
IRGEIFFFKD RFIWRTVTPR DKPMGPLLVA TFWPELPEKI DAVYEAPQEE KAVFFAGNEY

       550        560        570        580        590        600
WIYSASTLER GYPKPLTSLG LPPDVQRVDA AFNWSKNKKT YIFAGDKFWR YNEVKKKMDP

       610        620        630        640        650        660
GFPKLIADAW NAIPDNLDAV VDLQGGGHSY FFKGAYYLKL ENQSLKSVKF GSIKSDWLGC
```

The following domains have been identified in 72 kDa type IV collagenase:

Residues	Length	Domain ID
1-29	29	Signal peptide
30-109	90	Activation peptide
110-660	551	72 kDa type IV collagenase (4-73)

The human Metalloproteinase inhibitor 2 precursor (Swiss-Prot P16035 (SEQ ID NO: 4)) has the following sequence:

```
        10         20         30         40         50         60
MGAAARTLRL ALGLLLLATL LRPADACSCS PVHPQQAFCN ADVVIRAKAV SEKEVDSGND

        70         80         90        100        110        120
IYGNPIKRIQ YEIKQIKMFK GPEKDIEFIY TAPSSAVCGV SLDVGGKKEY LIAGKAEGDG

       130        140        150        160        170        180
KMHITLCDFI VPWDTLSTTQ KKSLNHRYQM GCECKITRCP MIPCYISSPD ECLWMDWVTE

       190        200        210        220
KNINGHQAKF FACIKRSDGS CAWYRGAAPP KQEFLDIEDP
```

The following domains have been identified in Metalloproteinase inhibitor 2:

Residues	Length	Domain ID
1-26	26	Signal peptide
27-220	194	Metalloproteinase inhibitor 2

As used herein, the term "Insulin-like growth factor 1 receptor" refers to one or more polypeptides present in a biological sample that are derived from the Insulin-like growth factor 1 receptor precursor (Swiss-Prot P08069 (SEQ ID NO: 5)).

```
        10         20         30         40         50         60
MKSGSGGGSP TSLWGLLFLS AALSLWPTSG EICGPGIDIR NDYQQLKRLE NCTVIEGYLH

        70         80         90        100        110        120
ILLISKAEDY RSYRFPKLTV ITEYLLLFRV AGLESLGDLF PNLTVIRGWK LFYNYALVIF

       130        140        150        160        170        180
EMTNLKDIGL YNLRNITRGA IRIEKNADLC YLSTVDWSLI LDAVSNNYIV GNKPPKECGD

       190        200        210        220        230        240
LCPGTMEEKP MCEKTTINNE YNYRCWTTNR CQKMCPSTCG KRACTENNEC CHPECLGSCS

       250        260        270        280        290        300
APDNDTACVA CRHYYYAGVC VPACPPNTYR FEGWRCVDRD FCANILSAES SDSEGFVIHD

       310        320        330        340        350        360
GECMQECPSG FIRNGSQSMY CIPCEGPCPK VCEEEKKTKT IDSVTSAQML QGCTIFKGNL

       370        380        390        400        410        420
LINIRRGNNI ASELENFMGL IEVVTGYVKI RHSHALVSLS FLKNLRLILG EEQLEGNYSF

       430        440        450        460        470        480
YVLDNQNLQQ LWDWDHRNLT IKAGKMYFAF NPKLCVSEIY RMEEVTGTKG RQSKGDINTR

       490        500        510        520        530        540
NNGERASCES DVLHFTSTTT SKNRIIITWH RYRPPDYRDL ISFTVYYKEA PFKNVTEYDG

       550        560        570        580        590        600
QDACGSNSWN MVDVDLPPNK DVEPGILLHG LKPWTQYAVY VKAVTLTMVE NDHIRGAKSE

       610        620        630        640        650        660
ILYIRTNASV PSIPLDVLSA SNSSSQLIVK WNPPSLPNGN LSYYIVRWQR QPQDGYLYRH

       670        680        690        700        710        720
NYCSKDKIPI RKYADGTIDI EEVTENPKTE VCGGEKGPCC ACPKTEAEKQ AEKEEAEYRK

       730        740        750        760        770        780
VFENFLHNSI FVPRPERKRR DVMQVANTTM SSRSRNTTAA DTYNITDPEE LETEYPFFES

       790        800        810        820        830        840
RVDNKERTVI SNLRPFTLYR IDIHSCNHEA EKLGCSASNF VFARTMPAEG ADDIPGPVTW

       850        860        870        880        890        900
EPRPENSIFL KWPEPENPNG LILMYEIKYG SQVEDQRECV SRQEYRKYGG AKLNRLNPGN

       910        920        930        940        950        960
YTARIQATSL SGNGSWTDPV FFYVQAKTGY ENFIHLIIAL PVAVLLIVGG LVIMLYVFHR

       970        980        990       1000       1010       1020
KRNNSRLGNG VLYASVNPEY FSAADVYVPD EWEVAREKIT MSRELGQGSF GMVYEGVAKG

      1030       1040       1050       1060       1070       1080
VVKDEPETRV AIKTVNEAAS MRERIEFLNE ASVMKEFNCH HVVRLLGVVS QGQPTLVIME

      1090       1100       1110       1120       1130       1140
LMTRGDLKSY LRSLRPEMEN NPVLAPPSLS KMIQMAGEIA DGMAYLNANK FVHRDLAARN

      1150       1160       1170       1180       1190       1200
CMVAEDFTVK IGDFGMTRDI YETDYYRKGG KGLLPVRWMS PESLKDGVFT TYSDVWSFGV

      1210       1220       1230       1240       1250       1260
VLWEIATLAE QPYQGLSNEQ VLRFVMEGGL LDKPDNCPDM LFELMRMCWQ YNPKMRPSFL

      1270       1280       1290       1300       1310       1320
EIISSIKEEM EPGFREVSFY YSEENKLPEP EELDLEPENM ESVPLDPSAS SSSLPLPDRH

      1330       1340       1350       1360
SGHKAENGPG PGVLVLRASF DERQPYAHMN GGRKNERALP LPQSSTC
```

Most preferably, the Insulin-like growth factor 1 receptor assay detects one or more soluble forms of Insulin-like growth factor 1 receptor. Insulin-like growth factor 1 receptor is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of Insulin-like growth factor 1 receptor generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in Insulin-like growth factor 1 receptor:

Residues	Length	Domain ID
1-30	30	signal sequence
31-736	706	Insulin-like growth factor 1 receptor alpha chain (extracellular)
741-1367	627	Insulin-like growth factor 1 receptor beta chain
741-935	195	extracellular
936-959	24	transmembrane
960-1367	408	cytoplasmic

-continued

As used herein, the term "myeloid differentiation primary response protein MyD88" refers to one or more polypeptides present in a biological sample that are derived from the myeloid differentiation primary response protein MyD88 precursor (Swiss-Prot Q99836 (SEQ ID NO: 6)).

```
        10         20         30         40         50         60
MAAGGPGAGS AAPVSSTSSL PLAALNMRVR RRLSLFLNVR TQVAADWTAL AEEMDFEYLE

        70         80         90        100        110        120
IRQLETQADP TGRLLDAWQG RPGASVGRLL ELLTKLGRDD VLLELGPSIE EDCQKYILKQ

       130        140        150        160        170        180
QQEEAEKPLQ VAAVDSSVPR TAELAGITTL DDPLGHMPER FDAFICYCPS DIQFVQEMIR

       190        200        210        220        230        240
QLEQTNYRLK LCVSDRDVLP GTCVWSIASE LIEKRCRRMV VVVSDDYLQS KECDFQTKFA

       250        260        270        280        290
LSLSPGAHQK RLIPIKYKAM KKEFPSILRF ITVCDYTNPC TKSWFWTRLA KALSLP
```

As used herein, the term "neuronal cell adhesion molecule" refers to one or more polypeptides present in a biological sample that are derived from the neuronal cell adhesion molecule precursor (Swiss-Prot Q92823 (SEQ ID NO: 7)).

```
        10         20         30         40         50         60
MQLKIMPKKK RLSAGRVPLI LFLCQMISAL EVPLDPKLLE DLVQPPTITQ QSPKDYIIDP

        70         80         90        100        110        120
RENIVIQCEA KGKPPPSFSW TRNGTHFDID KDPLVTMKPG TGTLIINIMS EGKAETYEGV

       130        140        150        160        170        180
YQCTARNERG AAVSNNIVVR PSRSPLWTKE KLEPITLQSG QSLVLPCRPP IGLPPPIIFW

       190        200        210        220        230        240
MDNSFQRLPQ SERVSQGLNG DLYFSNVLPE DTREDYICYA RFNHTQTIQQ KQPISVKVIS

       250        260        270        280        290        300
VDELNDTIAA NLSDTEFYGA KSSRERPPTF LTPEGNASNK EELRGNVLSL ECIAEGLPTP

       310        320        330        340        350        360
IIYWAKEDGM LPKNRTVYKN FEKTLQIIHV SEADSGNYQC IAKNALGAIH HTISVRVKAA

       370        380        390        400        410        420
PYWITAPQNL VLSPGEDGTL ICRANGNPKP RISWLTNGVP IEIAPDDPSR KIDGDTIIFS

       430        440        450        460        470        480
NVQERSSAVY QCNASNEYGY LLANAFVNVL AEPPRILTPA NTLYQVIANR PALLDCAFFG

       490        500        510        520        530        540
SPLPTIEWFK GAKGSALHED IYVLHENGTL EIPVAQKDST GTYTCVARNK LGMAKNEVHL

       550        560        570        580        590        600
EIKDPTWIVK QPEYAVVQRG SMVSFECKVK HDHTLSLTVL WLKDNRELPS DERFTVDKDH

       610        620        630        640        650        660
LVVADVSDDD SGTYTCVANT TLDSVSASAV LSVVAPTPTP APVYDVPNPP FDLELTDQLD
```

-continued

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       670        680        690        700        710        720
KSVQLSWTPG DDNNSPITKF IIEYEDAMHK PGLWHHQTEV SGTQTTAQLK LSPYVNYSFR

       730        740        750        760        770        780
VMAVNSIGKS LPSEASEQYL TKASEPDKNP TAVEGLGSEP DNLVITWKPL NGFESNGPGL

       790        800        810        820        830        840
QYKVSWRQKD GDDEWTSVVV ANVSKYIVSG TPTFVPYLIK VQALNDMGFA PEPAVVMGHS

       850        860        870        880        890        900
GEDLPMVAPG NVRVNVVNST LAEVHWDPVP LKSIRGHLQG YRIYYWKTQS SSKRNRRHIE

       910        920        930        940        950        960
KKILTFQGSK THGMLPGLEP FSHYTLNVRV VNGKGEGPAS PDRVFNTPEG VPSAPSSLKI

       970        980        990       1000       1010       1020
VNPTLDSLTL EWDPPSHPNG ILTEYTLKYQ PINSTHELGP LVDLKIPANK TRWTLKNLNF

      1030       1040       1050       1060       1070       1080
STRYKFYFYA QTSAGSGSQI TEEAVTTVDE AGILPPDVGA GKVQAVNTRI SNLTAAAAET

      1090       1100       1110       1120       1130       1140
YANISWEYEG PEHVNFYVEY GVAGSKEEWR KEIVNGSRSF FGLKGLMPGT AYKVRVGAVG

      1150       1160       1170       1180       1190       1200
DSGFVSSEDV FETGPAMASR QVDIATQGWF IGLMCAVALL ILILLIVCFI RRNKGGKYPV

      1210       1220       1230       1240       1250       1260
KEKEDAHADP EIQPMKEDDG TFGEYSDAED HKPLKKGSRT PSDRTVKKED SDDSLVDYGE

      1270       1280       1290       1300
GVNGQFNEDG SFIGQYSGKK EKEPAEGNES SEAPSPVNAM NSFV
```

Most preferably, the neuronal cell adhesion molecule assay detects one or more soluble forms of neuronal cell adhesion molecule. The Neuronal cell adhesion molecule precursor encodes a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of neuronal cell adhesion molecule generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in neuronal cell adhesion molecule:

Residues	Length	Domain ID
1-24	24	signal sequence
25-1304	1280	neuronal cell adhesion molecule
25-1167	1143	extracellular
1168-1190	23	transmembrane
1191-1304	114	cytoplasmic

As used herein, the term "Tumor necrosis factor ligand superfamily member 10" refers to one or more polypeptides present in a biological sample that are derived from the Tumor necrosis factor ligand superfamily member 10 precursor (Swiss-Prot P50591 (SEQ ID NO: 8))

```
        10         20         30         40         50         60
MAMMEVQGGP SLGQTCVLIV IFTVLLQSLC VAVTYVYFTN ELKQMQDKYS KSGIACFLKE

        70         80         90        100        110        120
DDSYWDPNDE ESMNSPCWQV KWQLRQLVRK MILRTSEETI STVQEKQQNI SPLVRERGPQ

       130        140        150        160        170        180
RVAAHITGTR GRSNTLSSPN SKNEKALGRK INSWESSRSG HSFLSNLHLR NGELVIHEKG

       190        200        210        220        230        240
FYYIYSQTYF RFQEEIKENT KNDKQMVQYI YKYTSYPDPI LLMKSARNSC WSKDAEYGLY

       250        260        270        280
SIYQGGIFEL KENDRIFVSV TNEHLIDMDH EASFFGAFLV G
```

This protein is also known as TRAIL and APO2L. Most preferably, the Tumor necrosis factor ligand superfamily member 10 precursor assay detects one or more soluble forms of Tumor necrosis factor ligand superfamily member 10 precursor. The Tumor necrosis factor ligand superfamily member 10 precursor encodes a single-pass type II membrane protein having a large extracellular domain, most or all of which is present in soluble forms of Tumor necrosis factor ligand superfamily member 10 precursor generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in Tumor necrosis factor ligand superfamily member 10 precursor:

Residues	Length	Domain ID
1-281	281	Tumor necrosis factor ligand superfamily member 10
1-17	17	cytoplasmic domain
18-38	21	Signal-anchor for type II membrane protein
39-281	243	extracellular domain

As used herein, the term "alpha-1-antitrypsin:leukocyte elastase complex" refers to a polypeptide complex present in a biological sample that comprises one or more polypeptides that are derived from the alpha-1-antitrypsin precursor and one or more polypeptides that are derived from the leukocyte elastase precursor.

The human alpha-1-antitrypsin precursor has the following sequence (Swiss-Prot P01009 (SEQ ID NO: 9)):

```
        10         20         30         40         50         60
MPSSVSWGIL LLAGLCCLVP VSLAEDPQGD AAQKTDTSHH DQDHPTFNKI TPNLAEFAFS

        70         80         90        100        110        120
LYRQLAHQSN STNIFFSPVS IATAFAMLSL GTKADTHDEI LEGLNFNLTE IPEAQIHEGF

       130        140        150        160        170        180
QELLRTLNQP DSQLQLTTGN GLFLSEGLKL VDKFLEDVKK LYHSEAFTVN FGDTEEAKKQ

       190        200        210        220        230        240
INDYVEKGTQ GKIVDLVKEL DRDTVFALVN YIFFKGKWER PFEVKDTEEE DFHVDQVTTV

       250        260        270        280        290        300
KVPMMKRLGM FNIQHCKKLS SWVLLMKYLG NATAIFFLPD EGKLQHLENE LTHDIITKFL

       310        320        330        340        350        360
ENEDRRSASL HLPKLSITGT YDLKSVLGQL GITKVFSNGA DLSGVTEEAP LKLSKAVHKA

       370        380        390        400        410
VLTIDEKGTE AAGAMFLEAI PMSIPPEVKF NKPFVFLMIE QNTKSPLFMG KVVNPTQK
```

The following domains have been identified in alpha-1-antitrypsin:

Residues	Length	Domain ID
1-24	24	signal sequence
25-418	394	alpha-1-antitrypsin

The human leukocyte elastase precursor (Swiss-Prot P08246 (SEQ ID NO: 10)) has the following sequence:

```
        10         20         30         40         50         60
MTLGRRLACL FLACVLPALL LGGTALASEI VGGRRARPHA WPFMVSLQLR GGHFCGATLI

        70         80         90        100        110        120
APNFVMSAAH CVANVNVRAV RVVLGAHNLS RREPTRQVFA VQRIFENGYD PVNLLNDIVI

       130        140        150        160        170        180
LQLNGSATIN ANVQVAQLPA QGRRLGNGVQ CLAMGWGLLG RNRGIASVLQ ELNVTVVTSL

       190        200        210        220        230        240
CRRSNVCTLV RGRQAGVCFG DSGSPLVCNG LIHGIASFVR GGCASGLYPD AFAPVAQFVN

       250        260
WIDSIIQRSE DNPCPHPRDP DPASRTH
```

The following domains have been identified in leukocyte elastase:

Residues	Length	Domain ID
1-27	315	signal sequence
28-29	2	pro-peptide
30-267	238	leukocyte elastase

As used herein, the term "relating a signal to the presence or amount" of an analyte reflects the following understanding. Assay signals are typically related to the presence or amount of an analyte through the use of a standard curve calculated using known concentrations of the analyte of interest. As the term is used herein, an assay is "configured to detect" an analyte if an assay can generate a detectable signal indicative of the presence or amount of a physiologically relevant concentration of the analyte. Because an antibody epitope is on the order of 8 amino acids, an immunoassay configured to detect a marker of interest will also detect polypeptides related to the marker sequence, so long as those polypeptides contain the epitope(s) necessary to bind to the antibody or antibodies used in the assay. The term "related marker" as used herein with regard to a biomarker such as one of the kidney injury markers described herein refers to one or more fragments, variants, etc., of a particular marker or its biosynthetic parent that may be detected as a surrogate for the marker itself or as independent biomarkers. The term also refers to one or more polypeptides present in a biological sample that are derived from the biomarker precursor complexed to additional species, such as binding proteins, receptors, heparin, lipids, sugars, etc.

In this regard, the skilled artisan will understand that the signals obtained from an immunoassay are a direct result of complexes formed between one or more antibodies and the target biomolecule (i.e., the analyte) and polypeptides containing the necessary epitope(s) to which the antibodies bind. While such assays may detect the full length biomarker and the assay result be expressed as a concentration of a

biomarker of interest, the signal from the assay is actually a result of all such "immunoreactive" polypeptides present in the sample. Expression of biomarkers may also be determined by means other than immunoassays, including protein measurements (such as dot blots, western blots, chromatographic methods, mass spectrometry, etc.) and nucleic acid measurements (mRNA quantitation). This list is not meant to be limiting.

The term "positive going" marker as that term is used herein refer to a marker that is determined to be elevated in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition. The term "negative going" marker as that term is used herein refer to a marker that is determined to be reduced in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition.

The term "subject" as used herein refers to a human or non-human organism. Thus, the methods and compositions described herein are applicable to both human and veterinary disease. Further, while a subject is preferably a living organism, the invention described herein may be used in post-mortem analysis as well. Preferred subjects are humans, and most preferably "patients," which as used herein refers to living humans that are receiving medical care for a disease or condition. This includes persons with no defined illness who are being investigated for signs of pathology.

Preferably, an analyte is measured in a sample. Such a sample may be obtained from a subject, or may be obtained from biological materials intended to be provided to the subject. For example, a sample may be obtained from a kidney being evaluated for possible transplantation into a subject, and an analyte measurement used to evaluate the kidney for preexisting damage. Preferred samples are body fluid samples.

The term "body fluid sample" as used herein refers to a sample of bodily fluid obtained for the purpose of diagnosis, prognosis, classification or evaluation of a subject of interest, such as a patient or transplant donor. In certain embodiments, such a sample may be obtained for the purpose of determining the outcome of an ongoing condition or the effect of a treatment regimen on a condition. Preferred body fluid samples include blood, serum, plasma, cerebrospinal fluid, urine, saliva, sputum, and pleural effusions. In addition, one of skill in the art would realize that certain body fluid samples would be more readily analyzed following a fractionation or purification procedure, for example, separation of whole blood into serum or plasma components.

The term "diagnosis" as used herein refers to methods by which the skilled artisan can estimate and/or determine the probability ("a likelihood") of whether or not a patient is suffering from a given disease or condition. In the case of the present invention, "diagnosis" includes using the results of an assay, most preferably an immunoassay, for a kidney injury marker of the present invention, optionally together with other clinical characteristics, to arrive at a diagnosis (that is, the occurrence or nonoccurrence) of an acute renal injury or ARF for the subject from which a sample was obtained and assayed. That such a diagnosis is "determined" is not meant to imply that the diagnosis is 100% accurate. Many biomarkers are indicative of multiple conditions. The skilled clinician does not use biomarker results in an informational vacuum, but rather test results are used together with other clinical indicia to arrive at a diagnosis. Thus, a measured biomarker level on one side of a predetermined diagnostic threshold indicates a greater likelihood of the occurrence of disease in the subject relative to a measured level on the other side of the predetermined diagnostic threshold.

Similarly, a prognostic risk signals a probability ("a likelihood") that a given course or outcome will occur. A level or a change in level of a prognostic indicator, which in turn is associated with an increased probability of morbidity (e.g., worsening renal function, future ARF, or death) is referred to as being "indicative of an increased likelihood" of an adverse outcome in a patient.

Marker Assays

In general, immunoassays involve contacting a sample containing or suspected of containing a biomarker of interest with at least one antibody that specifically binds to the biomarker. A signal is then generated indicative of the presence or amount of complexes formed by the binding of polypeptides in the sample to the antibody. The signal is then related to the presence or amount of the biomarker in the sample. Numerous methods and devices are well known to the skilled artisan for the detection and analysis of biomarkers. See, e.g., U.S. Pat. Nos. 6,143,576; 6,113,855; 6,019,944; 5,985,579; 5,947,124; 5,939,272; 5,922,615; 5,885,527; 5,851,776; 5,824,799; 5,679,526; 5,525,524; and 5,480,792, and *The Immunoassay Handbook*, David Wild, ed. Stockton Press, New York, 1994, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims.

The assay devices and methods known in the art can utilize labeled molecules in various sandwich, competitive, or non-competitive assay formats, to generate a signal that is related to the presence or amount of the biomarker of interest. Suitable assay formats also include chromatographic, mass spectrographic, and protein "blotting" methods. Additionally, certain methods and devices, such as biosensors and optical immunoassays, may be employed to determine the presence or amount of analytes without the need for a labeled molecule. See, e.g., U.S. Pat. Nos. 5,631,171; and 5,955,377, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims. One skilled in the art also recognizes that robotic instrumentation including but not limited to Beckman ACCESS®, Abbott AXSYM®, Roche ELECSYS®, Dade Behring STRATUS® systems are among the immunoassay analyzers that are capable of performing immunoassays. But any suitable immunoassay may be utilized, for example, enzyme-linked immunoassays (ELISA), radioimmunoassays (RIAs), competitive binding assays, and the like.

Antibodies or other polypeptides may be immobilized onto a variety of solid supports for use in assays. Solid phases that may be used to immobilize specific binding members include those developed and/or used as solid phases in solid phase binding assays. Examples of suitable solid phases include membrane filters, cellulose-based papers, beads (including polymeric, latex and paramagnetic particles), glass, silicon wafers, microparticles, nanoparticles, TentaGels, AgroGels, PEGA gels, SPOCC gels, and multiple-well plates. An assay strip could be prepared by coating the antibody or a plurality of antibodies in an array on solid support. This strip could then be dipped into the test sample and then processed quickly through washes and detection steps to generate a measurable signal, such as a colored spot. Antibodies or other polypeptides may be bound to specific zones of assay devices either by conjugating directly to an assay device surface, or by indirect binding. In an example of the later case, antibodies or other

polypeptides may be immobilized on particles or other solid supports, and that solid support immobilized to the device surface.

Biological assays require methods for detection, and one of the most common methods for quantitation of results is to conjugate a detectable label to a protein or nucleic acid that has affinity for one of the components in the biological system being studied. Detectable labels may include molecules that are themselves detectable (e.g., fluorescent moieties, electrochemical labels, metal chelates, etc.) as well as molecules that may be indirectly detected by production of a detectable reaction product (e.g., enzymes such as horseradish peroxidase, alkaline phosphatase, etc.) or by a specific binding molecule which itself may be detectable (e.g., biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, etc.).

Preparation of solid phases and detectable label conjugates often comprise the use of chemical cross-linkers. Cross-linking reagents contain at least two reactive groups, and are divided generally into homofunctional cross-linkers (containing identical reactive groups) and heterofunctional cross-linkers (containing non-identical reactive groups). Homobifunctional cross-linkers that couple through amines, sulfhydryls or react non-specifically are available from many commercial sources. Maleimides, alkyl and aryl halides, alpha-haloacyls and pyridyl disulfides are thiol reactive groups. Maleimides, alkyl and aryl halides, and alpha-haloacyls react with sulfhydryls to form thiol ether bonds, while pyridyl disulfides react with sulfhydryls to produce mixed disulfides. The pyridyl disulfide product is cleavable. Imidoesters are also very useful for protein-protein cross-links. A variety of heterobifunctional cross-linkers, each combining different attributes for successful conjugation, are commercially available.

In certain aspects, the present invention provides kits for the analysis of the described kidney injury markers. The kit comprises reagents for the analysis of at least one test sample which comprise at least one antibody that a kidney injury marker. The kit can also include devices and instructions for performing one or more of the diagnostic and/or prognostic correlations described herein. Preferred kits will comprise an antibody pair for performing a sandwich assay, or a labeled species for performing a competitive assay, for the analyte. Preferably, an antibody pair comprises a first antibody conjugated to a solid phase and a second antibody conjugated to a detectable label, wherein each of the first and second antibodies that bind a kidney injury marker. Most preferably each of the antibodies are monoclonal antibodies. The instructions for use of the kit and performing the correlations can be in the form of labeling, which refers to any written or recorded material that is attached to, or otherwise accompanies a kit at any time during its manufacture, transport, sale or use. For example, the term labeling encompasses advertising leaflets and brochures, packaging materials, instructions, audio or video cassettes, computer discs, as well as writing imprinted directly on kits.

Antibodies

The term "antibody" as used herein refers to a peptide or polypeptide derived from, modeled after or substantially encoded by an immunoglobulin gene or immunoglobulin genes, or fragments thereof, capable of specifically binding an antigen or epitope. See, e.g. Fundamental Immunology, 3rd Edition, W. E. Paul, ed., Raven Press, N.Y. (1993); Wilson (1994; J. Immunol. Methods 175:267-273; Yarmush (1992) J. Biochem. Biophys. Methods 25:85-97. The term antibody includes antigen-binding portions, i.e., "antigen binding sites," (e.g., fragments, subsequences, complementarity determining regions (CDRs)) that retain capacity to bind antigen, including (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward et al., (1989) Nature 341:544-546), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Single chain antibodies are also included by reference in the term "antibody."

Antibodies used in the immunoassays described herein preferably specifically bind to a kidney injury marker of the present invention. The term "specifically binds" is not intended to indicate that an antibody binds exclusively to its intended target since, as noted above, an antibody binds to any polypeptide displaying the epitope(s) to which the antibody binds. Rather, an antibody "specifically binds" if its affinity for its intended target is about 5-fold greater when compared to its affinity for a non-target molecule which does not display the appropriate epitope(s). Preferably the affinity of the antibody will be at least about 5 fold, preferably 10 fold, more preferably 25-fold, even more preferably 50-fold, and most preferably 100-fold or more, greater for a target molecule than its affinity for a non-target molecule. In preferred embodiments, Preferred antibodies bind with affinities of at least about 10^7 M^{-1}, and preferably between about 10^8 M^{-1} to about 10^9 M^{-1}, about 10^9 M^{-1} to about 10^{10} M^{-1}, or about 10^{10} M^{-1} to about 10^{12} M^{-1}.

Affinity is calculated as $K_d=k_{off}/k_{on}$ (k_{off} is the dissociation rate constant, K_{on} is the association rate constant and K_d is the equilibrium constant). Affinity can be determined at equilibrium by measuring the fraction bound (r) of labeled ligand at various concentrations (c). The data are graphed using the Scatchard equation: r/c=K(n−r): where r=moles of bound ligand/mole of receptor at equilibrium; c=free ligand concentration at equilibrium; K=equilibrium association constant; and n=number of ligand binding sites per receptor molecule. By graphical analysis, r/c is plotted on the Y-axis versus r on the X-axis, thus producing a Scatchard plot. Antibody affinity measurement by Scatchard analysis is well known in the art. See, e.g., van Erp et al., *J. Immunoassay* 12: 425-43, 1991; Nelson and Griswold, *Comput. Methods Programs Biomed.* 27: 65-8, 1988.

The term "epitope" refers to an antigenic determinant capable of specific binding to an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and non-conformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

Numerous publications discuss the use of phage display technology to produce and screen libraries of polypeptides for binding to a selected analyte. See, e.g, Cwirla et al., *Proc. Natl. Acad. Sci. USA* 87, 6378-82, 1990; Devlin et al., *Science* 249, 404-6, 1990, Scott and Smith, *Science* 249, 386-88, 1990; and Ladner et al., U.S. Pat. No. 5,571,698. A basic concept of phage display methods is the establishment of a physical association between DNA encoding a polypeptide to be screened and the polypeptide. This physical association is provided by the phage particle, which displays a polypeptide as part of a capsid enclosing the phage genome which encodes the polypeptide. The establishment of a physical association between polypeptides and their genetic

material allows simultaneous mass screening of very large numbers of phage bearing different polypeptides. Phage displaying a polypeptide with affinity to a target bind to the target and these phage are enriched by affinity screening to the target. The identity of polypeptides displayed from these phage can be determined from their respective genomes. Using these methods a polypeptide identified as having a binding affinity for a desired target can then be synthesized in bulk by conventional means. See, e.g., U.S. Pat. No. 6,057,098, which is hereby incorporated in its entirety, including all tables, figures, and claims.

The antibodies that are generated by these methods may then be selected by first screening for affinity and specificity with the purified polypeptide of interest and, if required, comparing the results to the affinity and specificity of the antibodies with polypeptides that are desired to be excluded from binding. The screening procedure can involve immobilization of the purified polypeptides in separate wells of microtiter plates. The solution containing a potential antibody or groups of antibodies is then placed into the respective microtiter wells and incubated for about 30 min to 2 h. The microtiter wells are then washed and a labeled secondary antibody (for example, an anti-mouse antibody conjugated to alkaline phosphatase if the raised antibodies are mouse antibodies) is added to the wells and incubated for about 30 min and then washed. Substrate is added to the wells and a color reaction will appear where antibody to the immobilized polypeptide(s) are present.

The antibodies so identified may then be further analyzed for affinity and specificity in the assay design selected. In the development of immunoassays for a target protein, the purified target protein acts as a standard with which to judge the sensitivity and specificity of the immunoassay using the antibodies that have been selected. Because the binding affinity of various antibodies may differ; certain antibody pairs (e.g., in sandwich assays) may interfere with one another sterically, etc., assay performance of an antibody may be a more important measure than absolute affinity and specificity of an antibody.

While the present application describes antibody-based binding assays in detail, alternatives to antibodies as binding species in assays are well known in the art. These include receptors for a particular target, aptamers, etc. Aptamers are oligonucleic acid or peptide molecules that bind to a specific target molecule. Aptamers are usually created by selecting them from a large random sequence pool, but natural aptamers also exist. High-affinity aptamers containing modified nucleotides conferring improved characteristics on the ligand, such as improved in vivo stability or improved delivery characteristics. Examples of such modifications include chemical substitutions at the ribose and/or phosphate and/or base positions, and may include amino acid side chain functionalities.

Assay Correlations

The term "correlating" as used herein in reference to the use of biomarkers refers to comparing the presence or amount of the biomarker(s) in a patient to its presence or amount in persons known to suffer from, or known to be at risk of, a given condition; or in persons known to be free of a given condition. Often, this takes the form of comparing an assay result in the form of a biomarker concentration to a predetermined threshold selected to be indicative of the occurrence or nonoccurrence of a disease or the likelihood of some future outcome.

Selecting a diagnostic threshold involves, among other things, consideration of the probability of disease, distribution of true and false diagnoses at different test thresholds, and estimates of the consequences of treatment (or a failure to treat) based on the diagnosis. For example, when considering administering a specific therapy which is highly efficacious and has a low level of risk, few tests are needed because clinicians can accept substantial diagnostic uncertainty. On the other hand, in situations where treatment options are less effective and more risky, clinicians often need a higher degree of diagnostic certainty. Thus, cost/benefit analysis is involved in selecting a diagnostic threshold.

Suitable thresholds may be determined in a variety of ways. For example, one recommended diagnostic threshold for the diagnosis of acute myocardial infarction using cardiac troponin is the 97.5th percentile of the concentration seen in a normal population. Another method may be to look at serial samples from the same patient, where a prior "baseline" result is used to monitor for temporal changes in a biomarker level.

Population studies may also be used to select a decision threshold. Receiver Operating Characteristic ("ROC") arose from the field of signal detection theory developed during World War II for the analysis of radar images, and ROC analysis is often used to select a threshold able to best distinguish a "diseased" subpopulation from a "nondiseased" subpopulation. A false positive in this case occurs when the person tests positive, but actually does not have the disease. A false negative, on the other hand, occurs when the person tests negative, suggesting they are healthy, when they actually do have the disease. To draw a ROC curve, the true positive rate (TPR) and false positive rate (FPR) are determined as the decision threshold is varied continuously. Since TPR is equivalent with sensitivity and FPR is equal to 1−specificity, the ROC graph is sometimes called the sensitivity vs (1−specificity) plot. A perfect test will have an area under the ROC curve of 1.0; a random test will have an area of 0.5. A threshold is selected to provide an acceptable level of specificity and sensitivity.

In this context, "diseased" is meant to refer to a population having one characteristic (the presence of a disease or condition or the occurrence of some outcome) and "nondiseased" is meant to refer to a population lacking the characteristic. While a single decision threshold is the simplest application of such a method, multiple decision thresholds may be used. For example, below a first threshold, the absence of disease may be assigned with relatively high confidence, and above a second threshold the presence of disease may also be assigned with relatively high confidence. Between the two thresholds may be considered indeterminate. This is meant to be exemplary in nature only.

In addition to threshold comparisons, other methods for correlating assay results to a patient classification (occurrence or nonoccurrence of disease, likelihood of an outcome, etc.) include decision trees, rule sets, Bayesian methods, and neural network methods. These methods can produce probability values representing the degree to which a subject belongs to one classification out of a plurality of classifications.

Measures of test accuracy may be obtained as described in Fischer et al., *Intensive Care Med.* 29: 1043-51, 2003, and used to determine the effectiveness of a given biomarker. These measures include sensitivity and specificity, predictive values, likelihood ratios, diagnostic odds ratios, and ROC curve areas. The area under the curve ("AUC") of a ROC plot is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one. The area under the ROC curve may be thought of as equivalent to the Mann-Whitney U test, which

tests for the median difference between scores obtained in the two groups considered if the groups are of continuous data, or to the Wilcoxon test of ranks.

As discussed above, suitable tests may exhibit one or more of the following results on these various measures: a specificity of greater than 0.5, preferably at least 0.6, more preferably at least 0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding sensitivity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; a sensitivity of greater than 0.5, preferably at least 0.6, more preferably at least 0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding specificity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; at least 75% sensitivity, combined with at least 75% specificity; a ROC curve area of greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95; an odds ratio different from 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less; a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least 2, more preferably at least 3, still more preferably at least 5, and most preferably at least 10; and or a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal to 0.5, more preferably less than or equal to 0.3, and most preferably less than or equal to 0.1

Additional clinical indicia may be combined with the kidney injury marker assay result(s) of the present invention. These include other biomarkers related to renal status. Examples include the following, which recite the common biomarker name, followed by the Swiss-Prot entry number for that biomarker or its parent: Actin (P68133); Adenosine deaminase binding protein (DPP4, P27487); Alpha-1-acid glycoprotein 1 (P02763); Alpha-1-microglobulin (P02760); Albumin (P02768); Angiotensinogenase (Renin, P00797); Annexin A2 (P07355); Beta-glucuronidase (P08236); B-2-microglobulin (P61679); Beta-galactosidase (P16278); BMP-7 (P18075); Brain natriuretic peptide (proBNP, BNP-32, NTproBNP; P16860); Calcium-binding protein Beta (S100-beta, P04271); Carbonic anhydrase (Q16790); Casein Kinase 2 (P68400); Ceruloplasmin (P00450); Clusterin (P10909); Complement C3 (P01024); Cysteine-rich protein (CYR61, O00622); Cytochrome C (P99999); Epidermal growth factor (EGF, P01133); Endothelin-1 (P05305); Exosomal Fetuin-A (P02765); Fatty acid-binding protein, heart (FABP3, P05413); Fatty acid-binding protein, liver (P07148); Ferritin (light chain, P02793; heavy chain P02794); Fructose-1,6-biphosphatase (P09467); GRO-alpha (CXCL1, (P09341); Growth Hormone (P01241); Hepatocyte growth factor (P14210); Insulin-like growth factor I (P01343); Immunoglobulin G; Immunoglobulin Light Chains (Kappa and Lambda); Interferon gamma (P01308); Lysozyme (P61626); Interleukin-1alpha (P01583); Interleukin-2 (P60568); Interleukin-4 (P60568); Interleukin-9 (P15248); Interleukin-12p40 (P29460); Interleukin-13 (P35225); Interleukin-16 (Q14005); L1 cell adhesion molecule (P32004); Lactate dehydrogenase (P00338); Leucine Aminopeptidase (P28838); Meprin A-alpha subunit (Q16819); Meprin A-beta subunit (Q16820); Midkine (P21741); MIP2-alpha (CXCL2, P19875); MMP-2 (P08253); MMP-9 (P14780); Netrin-1 (O95631); Neutral endopeptidase (P08473); Osteopontin (P10451); Renal papillary antigen 1 (RPA1); Renal papillary antigen 2 (RPA2); Retinol binding protein (P09455); Ribonuclease; 5100 calcium-binding protein A6 (P06703); Serum Amyloid P Component (P02743); Sodium/Hydrogen exchanger isoform (NHE3, P48764); Spermidine/spermine N1-acetyltransferase (P21673); TGF-Beta1 (P01137); Transferrin (P02787); Trefoil factor 3 (TFF3, Q07654); Toll-Like protein 4 (O00206); Total protein; Tubulointerstitial nephritis antigen (Q9UJW2); Uromodulin (Tamm-Horsfall protein, P07911).

For purposes of risk stratification, Adiponectin (Q15848); Alkaline phosphatase (P05186); Aminopeptidase N (P15144); CalbindinD28k (P05937); Cystatin C (P01034); 8 subunit of FIFO ATPase (P03928); Gamma-glutamyltransferase (P19440); GSTa (alpha-glutathione-S-transferase, P08263); GSTpi (Glutathione-S-transferase P; GST class-pi; P09211); IGFBP-1 (P08833); IGFBP-2 (P18065); IGFBP-6 (P24592); Integral membrane protein 1 (Itm1, P46977); Interleukin-6 (P05231); Interleukin-8 (P10145); Interleukin-18 (Q14116); IP-10 (10 kDa interferon-gamma-induced protein, P02778); IRPR (IFRD1, O00458); Isovaleryl-CoA dehydrogenase (IVD, P26440); I-TAC/CXCL11 (O14625); Keratin 19 (P08727); Kim-1 (Hepatitis A virus cellular receptor 1, O43656); L-arginine:glycine amidinotransferase (P50440); Leptin (P41159); Lipocalin2 (NGAL, P80188); MCP-1 (P13500); MIG (Gamma-interferon-induced monokine Q07325); MIP-1a (P10147); MIP-3a (P78556); MIP-1beta (P13236); MIP-1d (Q16663); NAG (N-acetyl-beta-D-glucosaminidase, P54802); Organic ion transporter (OCT2, O15244); Osteoprotegerin (O14788); P8 protein (O60356); Plasminogen activator inhibitor 1 (PAI-1, P05121); ProANP(1-98) (P01160); Protein phosphatase 1-beta (PPI-beta, P62140); Rab GDI-beta (P50395); Renal kallikrein (Q86U61); RT1.B-1 (alpha) chain of the integral membrane protein (Q5Y7A8); Soluble tumor necrosis factor receptor superfamily member 1A (sTNFR-I, P19438); Soluble tumor necrosis factor receptor superfamily member 1B (sTNFR-II, P20333); Tissue inhibitor of metalloproteinases 3 (TIMP-3, P35625); uPAR (Q03405) may be combined with the kidney injury marker assay result(s) of the present invention.

Other clinical indicia which may be combined with the kidney injury marker assay result(s) of the present invention includes demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (e.g., blood pressure, temperature, respiration rate), risk scores (APACHE score, PRE-DICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score), a urine total protein measurement, a glomerular filtration rate, an estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a renal papillary antigen 1 (RPA1)

measurement; a renal papillary antigen 2 (RPA2) measurement; a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatinine ratio, and/or a renal failure index calculated as urine sodium/(urine creatinine/plasma creatinine). Other measures of renal function which may be combined with the kidney injury marker assay result(s) are described hereinafter and in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

Combining assay results/clinical indicia in this manner can comprise the use of multivariate logistical regression, log linear modeling, neural network analysis, n-of-m analysis, decision tree analysis, etc. This list is not meant to be limiting.

Diagnosis of Acute Renal Failure

As noted above, the terms "acute renal (or kidney) injury" and "acute renal (or kidney) failure" as used herein are defined in part in terms of changes in serum creatinine from a baseline value. Most definitions of ARF have common elements, including the use of serum creatinine and, often, urine output. Patients may present with renal dysfunction without an available baseline measure of renal function for use in this comparison. In such an event, one may estimate a baseline serum creatinine value by assuming the patient initially had a normal GFR. Glomerular filtration rate (GFR) is the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time. Glomerular filtration rate (GFR) can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys. GFR is typically expressed in units of ml/min:

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

By normalizing the GFR to the body surface area, a GFR of approximately 75-100 ml/min per 1.73 m^2 can be assumed. The rate therefore measured is the quantity of the substance in the urine that originated from a calculable volume of blood.

There are several different techniques used to calculate or estimate the glomerular filtration rate (GFR or eGFR). In clinical practice, however, creatinine clearance is used to measure GFR. Creatinine is produced naturally by the body (creatinine is a metabolite of creatine, which is found in muscle). It is freely filtered by the glomerulus, but also actively secreted by the renal tubules in very small amounts such that creatinine clearance overestimates actual GFR by 10-20%. This margin of error is acceptable considering the ease with which creatinine clearance is measured.

Creatinine clearance (CCr) can be calculated if values for creatinine's urine concentration (U_{Cr}), urine flow rate (V), and creatinine's plasma concentration (P_{Cr}) are known. Since the product of urine concentration and urine flow rate yields creatinine's excretion rate, creatinine clearance is also said to be its excretion rate ($U_{Cr} \times V$) divided by its plasma concentration. This is commonly represented mathematically as:

$$C_{Cr} = \frac{U_{Cr} \times V}{P_{Cr}}$$

Commonly a 24 hour urine collection is undertaken, from empty-bladder one morning to the contents of the bladder the following morning, with a comparative blood test then taken:

$$C_{Cr} = \frac{U_{Cr} \times \text{24- hour volume}}{P_{Cr} \times 24 \times 60\ mins}$$

To allow comparison of results between people of different sizes, the CCr is often corrected for the body surface area (BSA) and expressed compared to the average sized man as ml/min/1.73 m2. While most adults have a BSA that approaches 1.7 (1.6-1.9), extremely obese or slim patients should have their CCr corrected for their actual BSA:

$$C_{Cr\text{- corrected}} = \frac{C_{Cr} \times 1.73}{BSA}$$

The accuracy of a creatinine clearance measurement (even when collection is complete) is limited because as glomerular filtration rate (GFR) falls creatinine secretion is increased, and thus the rise in serum creatinine is less. Thus, creatinine excretion is much greater than the filtered load, resulting in a potentially large overestimation of the GFR (as much as a twofold difference). However, for clinical purposes it is important to determine whether renal function is stable or getting worse or better. This is often determined by monitoring serum creatinine alone. Like creatinine clearance, the serum creatinine will not be an accurate reflection of GFR in the non-steady-state condition of ARF. Nonetheless, the degree to which serum creatinine changes from baseline will reflect the change in GFR. Serum creatinine is readily and easily measured and it is specific for renal function.

For purposes of determining urine output on a Urine output on a mL/kg/hr basis, hourly urine collection and measurement is adequate. In the case where, for example, only a cumulative 24-h output was available and no patient weights are provided, minor modifications of the RIFLE urine output criteria have been described. For example, Bagshaw et al., *Nephrol. Dial. Transplant.* 23: 1203-1210, 2008, assumes an average patient weight of 70 kg, and patients are assigned a RIFLE classification based on the following: <35 mL/h (Risk), <21 mL/h (Injury) or <4 mL/h (Failure).

Selecting a Treatment Regimen

Once a diagnosis is obtained, the clinician can readily select a treatment regimen that is compatible with the diagnosis, such as initiating renal replacement therapy, withdrawing delivery of compounds that are known to be damaging to the kidney, kidney transplantation, delaying or avoiding procedures that are known to be damaging to the kidney, modifying diuretic administration, initiating goal directed therapy, etc. The skilled artisan is aware of appropriate treatments for numerous diseases discussed in relation to the methods of diagnosis described herein. See, e.g., Merck Manual of Diagnosis and Therapy, 17th Ed. Merck Research Laboratories, Whitehouse Station, N.J., 1999. In addition, since the methods and compositions described

herein provide prognostic information, the markers of the present invention may be used to monitor a course of treatment. For example, improved or worsened prognostic state may indicate that a particular treatment is or is not efficacious.

One skilled in the art readily appreciates that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention.

Example 1

Contrast-Induced Nephropathy Sample Collection

The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after receiving intravascular contrast media. Approximately 250 adults undergoing radiographic/angiographic procedures involving intravascular administration of iodinated contrast media are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing a radiographic/angiographic procedure (such as a CT scan or coronary intervention) involving the intravascular administration of contrast media;

expected to be hospitalized for at least 48 hours after contrast administration.

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

renal transplant recipients;

acutely worsening renal function prior to the contrast procedure;

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

expected to undergo a major surgical procedure (such as involving cardiopulmonary bypass) or an additional imaging procedure with contrast media with significant risk for further renal insult within the 48 hrs following contrast administration;

participation in an interventional clinical study with an experimental therapy within the previous 30 days;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

Immediately prior to the first contrast administration (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL) and a urine sample (10 mL) are collected from each patient. Blood and urine samples are then collected at 4 (±0.5), 8 (±1), 24 (±2) 48 (±2), and 72 (±2) hrs following the last administration of contrast media during the index contrast procedure. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, Calif. The study urine samples are frozen and shipped to Astute Medical, Inc.

Serum creatinine is assessed at the site immediately prior to the first contrast administration (after any pre-procedure hydration) and at 4 (±0.5), 8 (±1), 24 (±2) and 48 (±2)), and 72 (±2) hours following the last administration of contrast (ideally at the same time as the study samples are obtained). In addition, each patient's status is evaluated through day 30 with regard to additional serum and urine creatinine measurements, a need for dialysis, hospitalization status, and adverse clinical outcomes (including mortality).

Prior to contrast administration, each patient is assigned a risk based on the following assessment: systolic blood pressure <80 mm Hg=5 points; intra-arterial balloon pump=5 points; congestive heart failure (Class III-IV or history of pulmonary edema)=5 points; age >75 yrs=4 points; hematocrit level <39% for men, <35% for women=3 points; diabetes=3 points; contrast media volume=1 point for each 100 mL; serum creatinine level >1.5 g/dL=4 points OR estimated GFR 40-60 mL/min/1.73 m^2=2 points, 20-40 mL/min/1.73 m^2=4 points, <20 mL/min/1.73 m^2=6 points. The risks assigned are as follows: risk for CIN and dialysis: 5 or less total points=risk of CIN—7.5%, risk of dialysis—0.04%; 6-10 total points=risk of CIN—14%, risk of dialysis—0.12%; 11-16 total points=risk of CIN—26.1%, risk of dialysis—1.09%; >16 total points=risk of CIN—57.3%, risk of dialysis—12.8%.

Example 2

Cardiac Surgery Sample Collection

The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after undergoing cardiovascular surgery, a procedure known to be potentially damaging to kidney function. Approximately 900 adults undergoing such surgery are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing cardiovascular surgery;

Toronto/Ottawa Predictive Risk Index for Renal Replacement risk score of at least 2 (Wijeysundera et al., *JAMA* 297: 1801-9, 2007); and

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

known pregnancy;

previous renal transplantation;

acutely worsening renal function prior to enrollment (e.g., any category of RIFLE criteria);

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

currently enrolled in another clinical study or expected to be enrolled in another clinical study within 7 days of cardiac surgery that involves drug infusion or a therapeutic intervention for AKI;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

Within 3 hours prior to the first incision (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL), whole blood (3 mL), and a urine sample (35 mL) are collected from each patient. Blood and urine samples are then collected at 3 (±0.5), 6 (±0.5), 12 (±1), 24 (±2) and 48 (±2) hrs following the procedure and then daily on days 3 through 7 if the subject remains in the hospital. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are frozen and shipped to Astute

Medical, Inc., San Diego, Calif. The study urine samples are frozen and shipped to Astute Medical, Inc.

Example 3

Acutely Ill Subject Sample Collection

The objective of this study is to collect samples from acutely ill patients. Approximately 1900 adults expected to be in the ICU for at least 48 hours will be enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

Study population 1: approximately 300 patients that have at least one of:

shock (SBP<90 mmHg and/or need for vasopressor support to maintain MAP>60 mmHg and/or documented drop in SBP of at least 40 mmHg); and

sepsis;

Study population 2: approximately 300 patients that have at least one of:

IV antibiotics ordered in computerized physician order entry (CPOE) within 24 hours of enrollment;

contrast media exposure within 24 hours of enrollment;

increased Intra-Abdominal Pressure with acute decompensated heart failure; and

severe trauma as the primary reason for ICU admission and likely to be hospitalized in the ICU for 48 hours after enrollment;

Study population 3: approximately 300 patients expected to be hospitalized through acute care setting (ICU or ED) with a known risk factor for acute renal injury (e.g. sepsis, hypotension/shock (Shock=systolic BP<90 mmHg and/or the need for vasopressor support to maintain a MAP>60 mmHg and/or a documented drop in SBP>40 mmHg), major trauma, hemorrhage, or major surgery); and/or expected to be hospitalized to the ICU for at least 24 hours after enrollment;

Study population 4: approximately 1000 patients that are 21 years of age or older, within 24 hours of being admitted into the ICU, expected to have an indwelling urinary catheter for at least 48 hours after enrollment, and have at least one of the following acute conditions within 24 hours prior to enrollment:

(i) respiratory SOFA score of ≥2 (PaO2/FiO2<300), (ii) cardiovascular SOFA score of ≥1 (MAP<70 mm Hg and/or any vasopressor required).

Exclusion Criteria

known pregnancy;

institutionalized individuals;

previous renal transplantation;

known acutely worsening renal function prior to enrollment (e.g., any category of RIFLE criteria);

received dialysis (either acute or chronic) within 5 days prior to enrollment or in imminent need of dialysis at the time of enrollment;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus;

meets any of the following:

(i) active bleeding with an anticipated need for >4 units PRBC in a day;

(ii) hemoglobin <7 g/dL;

(iii) any other condition that in the physician's opinion would contraindicate drawing serial blood samples for clinical study purposes;

meets only the SBP<90 mmHg inclusion criterion set forth above, and does not have shock in the attending physician's or principal investigator's opinion;

After obtaining informed consent, an EDTA anti-coagulated blood sample (10 mL) and a urine sample (25-50 mL) are collected from each patient. Blood and urine samples are then collected at 4 (±0.5) and 8 (±1) hours after contrast administration (if applicable); at 12 (±1), 24 (±2), 36 (±2), 48 (±2), 60 (±2), 72 (±2), and 84 (±2) hours after enrollment, and thereafter daily up to day 7 to day 14 while the subject is hospitalized. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, Calif. The study urine samples are frozen and shipped to Astute Medical, Inc.

Example 4

Immunoassay Format

Analytes are measured using standard sandwich enzyme immunoassay techniques. A first antibody which binds the analyte is immobilized in wells of a 96 well polystyrene microplate. Analyte standards and test samples are pipetted into the appropriate wells and any analyte present is bound by the immobilized antibody. After washing away any unbound substances, a horseradish peroxidase-conjugated second antibody which binds the analyte is added to the wells, thereby forming sandwich complexes with the analyte (if present) and the first antibody. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution comprising tetramethylbenzidine and hydrogen peroxide is added to the wells. Color develops in proportion to the amount of analyte present in the sample. The color development is stopped and the intensity of the color is measured at 540 nm or 570 nm. An analyte concentration is assigned to the test sample by comparison to a standard curve determined from the analyte standards.

Units for the concentrations reported in the following data tables are as follows: Heat shock 70 kDa protein 1—pg/mL, Alpha-1-antitrypsin Neutrophil elastase complex—pg/mL, Stromelysin-1:Metalloproteinase inhibitor 2 complex—pg/mL, Insulin-like growth factor 1 receptor—ng/mL, Myeloid differentiation primary response protein MyD88—ng/mL, Neuronal cell adhesion molecule—ng/mL, and Tumor necrosis factor ligand superfamily member 10—pg/mL. In the case of those kidney injury markers which are membrane proteins as described herein, the assays used in these examples detect soluble forms thereof.

Example 5

Apparently Healthy Donor and Chronic Disease Patient Samples

Human urine samples from donors with no known chronic or acute disease ("Apparently Healthy Donors") were purchased from two vendors (Golden West Biologicals, Inc., 27625 Commerce Center Dr., Temecula, Calif. 92590 and Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, Va. 23454). The urine samples were shipped and stored frozen at less than −20° C. The vendors supplied demographic information for the individual donors including gender, race (Black/White), smoking status and age.

Human urine samples from donors with various chronic diseases ("Chronic Disease Patients") including congestive heart failure, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus and hypertension were purchased from Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, Va. 23454. The urine samples were shipped and stored frozen at less than −20 degrees centigrade. The vendor provided a case report form for each individual donor with age, gender, race (Black/White), smoking status and alcohol use, height, weight, chronic disease(s) diagnosis, current medications and previous surgeries.

Example 6

Use of Kidney Injury Markers for Evaluating Renal Status in Patients

Patients from the intensive care unit (ICU) were enrolled in the following study. Each patient was classified by kidney status as non-injury (0), risk of injury (R), injury (I), and failure (F) according to the maximum stage reached within 7 days of enrollment as determined by the RIFLE criteria. EDTA anti-coagulated blood samples (10 mL) and a urine samples (25-30 mL) were collected from each patient at enrollment, 4 (±0.5) and 8 (±1) hours after contrast administration (if applicable); at 12 (±1), 24 (±2), and 48 (±2) hours after enrollment, and thereafter daily up to day 7 to day 14 while the subject is hospitalized. Markers were each measured by standard immunoassay methods using commercially available assay reagents in the urine samples and the plasma component of the blood samples collected.

Two cohorts were defined to represent a "diseased" and a "normal" population. While these terms are used for convenience, "diseased" and "normal" simply represent two cohorts for comparison (say RIFLE 0 vs RIFLE R, I and F; RIFLE 0 vs RIFLE R; RIFLE 0 and R vs RIFLE I and F; etc.). The time "prior max stage" represents the time at which a sample is collected, relative to the time a particular patient reaches the lowest disease stage as defined for that cohort, binned into three groups which are +/−12 hours. For example, "24 hr prior" which uses 0 vs R, I, F as the two cohorts would mean 24 hr (+/−12 hours) prior to reaching stage R (or I if no sample at R, or F if no sample at R or I).

A receiver operating characteristic (ROC) curve was generated for each biomarker measured and the area under each ROC curve (AUC) is determined Patients in Cohort 2 were also separated according to the reason for adjudication to cohort 2 as being based on serum creatinine measurements (sCr), being based on urine output (UO), or being based on either serum creatinine measurements or urine output. Using the same example discussed above (0 vs R, I, F), for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements alone, the stage 0 cohort may include patients adjudicated to stage R, I, or F on the basis of urine output; for those patients adjudicated to stage R, I, or F on the basis of urine output alone, the stage 0 cohort may include patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements; and for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements or urine output, the stage 0 cohort contains only patients in stage 0 for both serum creatinine measurements and urine output. Also, in the data for patients adjudicated on the basis of serum creatinine measurements or urine output, the adjudication method which yielded the most severe RIFLE stage is used.

The ability to distinguish cohort 1 from Cohort 2 was determined using ROC analysis. SE is the standard error of the AUC, n is the number of sample or individual patients ("pts," as indicated). Standard errors are calculated as described in Hanley, J. A., and McNeil, B. J., The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology (1982) 143: 29-36; p values are calculated with a two-tailed Z-test. An AUC<0.5 is indicative of a negative going marker for the comparison, and an AUC>0.5 is indicative of a positive going marker for the comparison.

Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 are determined OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

TABLE 1

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Stromelysin-1:Metalloproteinase inhibitor 2 complex						
	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.487	0.237	0.487	0.487	0.487	0.362
Average	328	5.13	328	22.4	328	0.362
Stdev	1910	21.0	1910	65.2	1910	0.176
p (t-test)		0.47		0.49		0.81
Min	0.237	0.237	0.237	0.237	0.237	0.237
Max	13900	91.7	13900	267	13900	0.487
n (Samp)	53	19	53	19	53	2
n (Patient)	42	19	42	19	42	2
sCr only						
Median	0.487	0.487	0.487	0.487	0.487	0.487
Average	193	0.387	193	111	193	0.487
Stdev	1440	0.137	1440	235	1440	0
p (t-test)		0.77		0.90		0.85
Min	0.237	0.237	0.237	0.237	0.237	0.487
Max	13900	0.487	13900	530	13900	0.487

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

n (Samp)	93	5	93	5	93	2
n (Patient)	73	5	73	5	73	2
UO only						
Median	0.487	0.237	0.487	0.487	0.487	0.487
Average	348	6.40	348	117	348	0.425
Stdev	2070	23.6	2070	431	2070	0.125
p (t-test)		0.53		0.62		0.74
Min	0.237	0.237	0.237	0.237	0.237	0.237
Max	13900	91.7	13900	1930	13900	0.487
n (Samp)	45	15	45	20	45	4
n (Patient)	35	15	35	20	35	4

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.32	0.47	0.39	0.44	0.57	0.58	0.35	0.63	0.54
SE	0.075	0.14	0.087	0.078	0.14	0.079	0.22	0.21	0.15
p	0.015	0.80	0.20	0.46	0.60	0.33	0.50	0.55	0.82
nCohort 1	53	93	45	53	93	45	53	93	45
nCohort 2	19	5	15	19	5	20	2	2	4
Cutoff 1	0	0	0	0	0	0.237	0	0.237	0.237
Sens 1	100%	100%	100%	100%	100%	70%	100%	100%	75%
Spec 1	0%	0%	0%	0%	0%	49%	0%	44%	49%
Cutoff 2	0	0	0	0	0	0	0	0.237	0
Sens 2	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 2	0%	0%	0%	0%	0%	0%	0%	44%	0%
Cutoff 3	0	0	0	0	0	0	0	0.237	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 3	0%	0%	0%	0%	0%	0%	0%	44%	0%
Cutoff 4	0.487	0.487	0.487	0.487	0.487	0.487	0.487	0.487	0.487
Sens 4	5%	0%	7%	21%	40%	25%	0%	0%	0%
Spec 4	77%	82%	78%	77%	82%	78%	77%	82%	78%
Cutoff 5	85.2	0.487	3.84	85.2	0.487	3.84	85.2	0.487	3.84
Sens 5	5%	0%	7%	11%	40%	25%	0%	0%	0%
Spec 5	81%	82%	80%	81%	82%	80%	81%	82%	80%
Cutoff 6	201	154	201	201	154	201	201	154	201
Sens 6	0%	0%	0%	5%	20%	10%	0%	0%	0%
Spec 6	91%	90%	93%	91%	90%	93%	91%	90%	93%
OR Quart 2	1.0	>3.6	5.1	0.70	0.96	>27	>0	>2.1	0
p Value	1.0	<0.29	0.17	0.67	0.98	<0.0044	<na	<0.56	na
95% CI of	0.058	>0.35	0.50	0.13	0.057	>2.8	>na	>0.18	na
OR Quart 2	17	na	52	3.7	16	na	na	na	na
OR Quart 3	34	>1.0	12	1.3	1.0	>7.3	>1.1	>0	3.7
p Value	0.0021	<0.98	0.030	0.70	1.0	<0.088	<0.96	<na	0.29
95% CI of	3.6	>0.062	1.3	0.30	0.059	>0.74	>0.061	>na	0.32
OR Quart 3	320	na	120	6.1	17	na	na	na	42
OR Quart 4	6.5	>1.1	3.5	2.2	2.0	>6.7	>1.2	>0	0
p Value	0.10	<0.95	0.30	0.28	0.58	<0.10	<0.92	<na	na
95% CI of	0.68	>0.064	0.32	0.52	0.17	>0.69	>0.066	>na	na
OR Quart4	63	na	38	9.6	24	na	na	na	na

Heat shock 70 kDa protein 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	277	424	277	499	277	225
Average	558	408	558	702	558	700
Stdev	1110	392	1110	906	1110	897
p (t-test)		0.58		0.62		0.83
Min	0.297	0.335	0.297	0.335	0.297	140
Max	7800	1680	7800	3860	7800	1730
n (Samp)	51	18	51	18	51	3
n (Patient)	41	18	41	18	41	3
sCr only						
Median	286	459	286	982	286	774
Average	535	863	535	861	535	774
Stdev	943	767	943	592	943	776
p (t-test)		0.45		0.45		0.72
Min	0.297	217	0.297	0.335	0.297	225

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Max	7800	1710	7800	1600	7800	1320
n (Samp)	90	5	90	5	90	2
n (Patient)	71	5	71	5	71	2
UO only						
Median	224	424	224	435	224	1680
Average	553	339	553	1260	553	1170
Stdev	1190	258	1190	2690	1190	801
p (t-test)		0.51		0.15		0.27
Min	0.297	0.335	0.297	0.335	0.297	140
Max	7800	812	7800	11800	7800	1820
n (Samp)	45	14	45	19	45	5
n (Patient)	35	14	35	19	35	5

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.52	0.68	0.53	0.57	0.70	0.64	0.57	0.69	0.78
SE	0.080	0.14	0.090	0.080	0.13	0.079	0.18	0.21	0.13
p	0.85	0.17	0.77	0.37	0.13	0.079	0.70	0.36	0.025
nCohort 1	51	90	45	51	90	45	51	90	45
nCohort 2	18	5	14	18	5	19	3	2	5
Cutoff 1	210	245	99.4	151	627	180	117	224	401
Sens 1	72%	80%	71%	72%	80%	74%	100%	100%	80%
Spec 1	39%	47%	36%	29%	73%	44%	29%	43%	67%
Cutoff 2	60.6	245	47.5	117	627	135	117	224	401
Sens 2	83%	80%	86%	83%	80%	84%	100%	100%	80%
Spec 2	20%	47%	24%	29%	73%	38%	29%	43%	67%
Cutoff 3	20.7	210	23.5	0.297	0.297	99.4	117	224	135
Sens 3	94%	100%	93%	100%	100%	95%	100%	100%	100%
Spec 3	10%	41%	16%	2%	1%	36%	29%	43%	38%
Cutoff 4	574	545	512	574	545	512	574	545	512
Sens 4	17%	40%	21%	44%	80%	42%	33%	50%	60%
Spec 4	71%	70%	71%	71%	70%	71%	71%	70%	71%
Cutoff 5	755	763	664	755	763	664	755	763	664
Sens 5	11%	40%	14%	33%	60%	32%	33%	50%	60%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	1020	1020	1320	1020	1020	1320	1020	1020	1320
Sens 6	6%	40%	0%	17%	40%	16%	33%	50%	60%
Spec 6	90%	90%	91%	90%	90%	91%	90%	90%	91%
OR Quart 2	1.0	>2.1	0.56	1.9	0	6.8	>2.2	>1.0	>1.0
p Value	1.0	<0.56	0.57	0.42	na	0.099	<0.55	<0.98	<1.0
95% CI of	0.20	>0.18	0.079	0.38	na	0.69	>0.17	>0.062	>0.056
OR Quart 2	4.9	na	4.0	9.9	na	67	na	na	na
OR Quart 3	2.3	>1.0	3.2	1.4	0.96	12	>0	>0	>1.1
p Value	0.28	<1.0	0.16	0.67	0.98	0.033	<na	<na	<0.95
95% CI of	0.52	>0.059	0.63	0.27	0.056	1.2	>na	>na	>0.061
OR Quart 3	10.0	na	16	7.7	16	110	na	na	na
OR Quart 4	0.65	>2.1	0.56	2.3	3.1	9.0	>1.0	>1.0	>3.6
p Value	0.61	<0.56	0.57	0.30	0.34	0.057	<1.0	<0.98	<0.30
95% CI of	0.12	>0.18	0.079	0.48	0.30	0.94	>0.056	>0.062	>0.32
OR Quart 4	3.5	na	4.0	11	33	87	na	na	na

Insulin-like growth factor 1 receptor

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0103	0.0103	0.0103	0.0169	nd	nd
Average	0.0275	0.0137	0.0275	0.0405	nd	nd
Stdev	0.0922	0.0113	0.0922	0.0818	nd	nd
p (t-test)		0.54		0.59	nd	nd
Min	0.000123	0.000172	0.000123	0.000172	nd	nd
Max	0.679	0.0423	0.679	0.365	nd	nd
n (Samp)	54	17	54	19	nd	nd
n (Patient)	43	17	43	19	nd	nd
sCr only						
Median	0.0103	0.00132	0.0103	0.0381	0.0103	0.0292
Average	0.0278	0.00733	0.0278	0.0354	0.0278	0.0292
Stdev	0.0804	0.00927	0.0804	0.0263	0.0804	0
p (t-test)		0.57		0.83		0.98

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Min	0.000123	0.000172	0.000123	0.000519	0.000123	0.0292
Max	0.679	0.0197	0.679	0.0680	0.679	0.0292
n (Samp)	91	5	91	5	91	2
n (Patient)	73	5	73	5	73	2
UO only						
Median	0.0103	0.0169	0.0103	0.0115	0.0103	0.0150
Average	0.0292	0.0166	0.0292	0.0335	0.0292	0.0200
Stdev	0.0988	0.0108	0.0988	0.0799	0.0988	0.0216
p (t-test)		0.65		0.86		0.87
Min	0.000123	0.000519	0.000123	0.000172	0.000123	0.00132
Max	0.679	0.0423	0.679	0.365	0.679	0.0436
n (Samp)	47	13	47	20	47	3
n (Patient)	37	13	37	20	37	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.50	0.34	0.59	0.59	0.72	0.56	nd	0.81	0.63
SE	0.081	0.14	0.092	0.078	0.13	0.078	nd	0.19	0.18
p	0.98	0.25	0.33	0.23	0.10	0.47	nd	0.093	0.48
nCohort 1	54	91	47	54	91	47	nd	91	47
nCohort 2	17	5	13	19	5	20	nd	2	3
Cutoff 1	0.00573	0.000172	0.00454	0.00132	0.0169	0.00454	nd	0.0254	0.000519
Sens 1	76%	80%	92%	74%	80%	70%	nd	100%	100%
Spec 1	30%	11%	36%	26%	67%	36%	nd	79%	30%
Cutoff 2	0.000519	0.000172	0.00454	0.000172	0.0169	0.000519	nd	0.0254	0.000519
Sens 2	82%	80%	92%	89%	80%	85%	nd	100%	100%
Spec 2	20%	11%	36%	13%	67%	30%	nd	79%	30%
Cutoff 3	0.000172	0.000123	0.00454	0.000123	0.000172	0.000172	nd	0.0254	0.000519
Sens 3	94%	100%	92%	100%	100%	90%	nd	100%	100%
Spec 3	13%	2%	36%	4%	11%	19%	nd	79%	30%
Cutoff 4	0.0169	0.0197	0.0169	0.0169	0.0197	0.0169	nd	0.0197	0.0169
Sens 4	35%	0%	46%	47%	60%	35%	nd	100%	33%
Spec 4	72%	71%	70%	72%	71%	70%	nd	71%	70%
Cutoff 5	0.0292	0.0292	0.0292	0.0292	0.0292	0.0292	nd	0.0292	0.0292
Sens 5	6%	0%	8%	32%	60%	15%	nd	0%	33%
Spec 5	85%	84%	85%	85%	84%	85%	nd	84%	85%
Cutoff 6	0.0388	0.0423	0.0388	0.0388	0.0423	0.0388	nd	0.0423	0.0388
Sens 6	6%	0%	8%	21%	40%	10%	nd	0%	33%
Spec 6	93%	92%	91%	93%	92%	91%	nd	92%	91%
OR Quart 2	1.2	>2.2	7.0	1.0	0	3.8	nd	>0	>1.0
p Value	0.77	<0.54	0.097	1.0	na	0.14	nd	<na	<1.0
95% CI of	0.27	>0.18	0.71	0.21	na	0.64	nd	>na	>0.056
OR Quart 2	5.7	na	69	4.8	na	23	nd	na	na
OR Quart 3	0.93	>0	3.5	1.0	1.0	3.8	nd	>0	>1.1
p Value	0.93	<na	0.30	1.0	1.0	0.14	nd	<na	<0.95
95% CI of	0.19	>na	0.32	0.21	0.059	0.64	nd	>na	>0.061
OR Quart 3	4.5	na	38	4.8	17	23	nd	na	na
OR Quart 4	0.93	>3.4	5.1	2.0	3.3	3.8	nd	>2.1	>1.0
p Value	0.93	<0.30	0.17	0.33	0.32	0.14	nd	<0.56	<1.0
95% CI of	0.19	>0.33	0.50	0.48	0.32	0.64	nd	>0.18	>0.056
OR Quart 4	4.5	na	52	8.7	34	23	nd	na	na

Interstitial collagenase:Metalloproteinase inhibitor 2 complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.233	0.233	0.233	0.233	0.233	0.231
Average	315	0.967	315	18.9	315	0.231
Stdev	2200	3.21	2200	68.2	2200	0.00389
p (t-test)		0.54		0.56		0.84
Min	0.228	0.228	0.228	0.228	0.228	0.228
Max	16000	14.2	16000	297	16000	0.233
n (Samp)	53	19	53	19	53	2
n (Patient)	42	19	42	19	42	2
sCr only						
Median	0.233	0.233	0.233	0.233	0.233	0.228
Average	184	4.37	184	6.08	184	0.228
Stdev	1660	6.22	1660	13.1	1660	0

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

p (t-test)		0.81		0.81		0.88
Min	0.228	0.228	0.228	0.228	0.228	0.228
Max	16000	14.2	16000	29.5	16000	0.228
n (Samp)	93	5	93	5	93	2
n (Patient)	73	5	73	5	73	2
UO only						
Median	0.233	0.233	0.233	0.233	0.233	0.231
Average	360	0.232	360	37.2	360	3.72
Stdev	2380	0.00268	2380	105	2380	6.99
p (t-test)		0.56		0.55		0.77
Min	0.228	0.228	0.228	0.228	0.228	0.228
Max	16000	0.233	16000	384	16000	14.2
n (Samp)	45	15	45	20	45	4
n (Patient)	35	15	35	20	35	4

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.50	0.61	0.40	0.58	0.56	0.50	0.42	0.18	0.42
SE	0.078	0.14	0.087	0.078	0.14	0.078	0.22	0.18	0.16
p	0.96	0.41	0.25	0.33	0.65	0.98	0.71	0.086	0.63
nCohort 1	53	93	45	53	93	45	53	93	45
nCohort 2	19	5	15	19	5	20	2	2	4
Cutoff 1	0	0.228	0	0.228	0.228	0	0	0	0
Sens 1	100%	80%	100%	74%	80%	100%	100%	100%	100%
Spec 1	0%	37%	0%	45%	37%	0%	0%	0%	0%
Cutoff 2	0	0.228	0	0	0.228	0	0	0	0
Sens 2	100%	80%	100%	100%	80%	100%	100%	100%	100%
Spec 2	0%	37%	0%	0%	37%	0%	0%	0%	0%
Cutoff 3	0	0	0	0	0	0	0	0	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 3	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 4	0.233	0.233	0.233	0.233	0.233	0.233	0.233	0.233	0.233
Sens 4	5%	40%	0%	26%	20%	30%	0%	0%	25%
Spec 4	77%	78%	73%	77%	78%	73%	77%	78%	73%
Cutoff 5	2.99	2.13	2.99	2.99	2.13	2.99	2.99	2.13	2.99
Sens 5	5%	40%	0%	21%	20%	25%	0%	0%	25%
Spec 5	81%	81%	80%	81%	81%	80%	81%	81%	80%
Cutoff 6	30.3	18.5	18.5	30.3	18.5	18.5	30.3	18.5	18.5
Sens 6	0%	0%	0%	11%	20%	15%	0%	0%	0%
Spec 6	91%	90%	93%	91%	90%	93%	91%	90%	93%
OR Quart 2	0.12	>1.0	>10	0	>1.0	0.43	>1.1	>0	1.1
p Value	0.061	<1.0	<0.047	na	<1.0	0.27	<0.96	<na	0.95
95% CI of	0.012	>0.059	>1.0	na	>0.059	0.095	>0.061	>na	0.061
OR Quart 2	1.1	na	na	na	na	1.9	na	na	20
OR Quart 3	3.1	>2.2	>5.5	2.6	>3.4	0.30	>0	>0	0
p Value	0.100	<0.54	<0.15	0.18	<0.30	0.14	<na	<na	na
95% CI of	0.80	>0.18	>0.53	0.65	>0.33	0.060	>na	>na	na
OR Quart 3	12	na	na	10	na	1.5	na	na	na
OR Quart 4	0.12	>2.1	>7.5	1.0	>1.0	0.70	>1.2	>2.3	2.4
p Value	0.061	<0.56	<0.085	1.0	<1.0	0.62	<0.92	<0.51	0.50
95% CI of	0.012	>0.18	>0.76	0.23	>0.059	0.17	>0.066	>0.19	0.19
OR Quart 4	1.1	na	na	4.3	na	2.8	na	na	31

72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	63.6	11.3	63.6	82.5	nd	nd
Average	610	807	610	1160	nd	nd
Stdev	2290	2050	2290	3840	nd	nd
p (t-test)		0.74		0.48	nd	nd
Min	1.15	1.15	1.15	1.15	nd	nd
Max	16000	8520	16000	16000	nd	nd
n (Samp)	50	19	50	17	nd	nd
n (Patient)	40	19	40	17	nd	nd
sCr only						
Median	34.8	29.2	34.8	292	34.8	918
Average	736	628	736	509	736	918

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Stdev	2550	1220	2550	670	2550	1230
p (t-test)		0.92		0.86		0.92
Min	1.15	1.19	1.15	1.19	1.15	51.6
Max	16000	3060	16000	1450	16000	1780
n (Samp)	88	6	88	4	88	2
n (Patient)	72	6	72	4	72	2
UO only						
Median	21.1	1.19	21.1	158	21.1	3060
Average	607	816	607	1240	607	4730
Stdev	2400	2210	2400	3680	2400	5730
p (t-test)		0.77		0.41		0.012
Min	1.15	1.15	1.15	1.15	1.15	30.3
Max	16000	8520	16000	16000	16000	11100
n (Samp)	45	15	45	19	45	3
n (Patient)	35	15	35	19	35	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.52	0.59	0.53	0.54	0.64	0.55	nd	0.72	0.82
SE	0.079	0.13	0.087	0.082	0.15	0.080	nd	0.21	0.15
p	0.85	0.49	0.73	0.62	0.37	0.51	nd	0.30	0.033
nCohort 1	50	88	45	50	88	45	nd	88	45
nCohort 2	19	6	15	17	4	19	nd	2	3
Cutoff 1	1.15	1.19	1.15	1.15	36.4	1.15	nd	36.4	21.1
Sens 1	95%	83%	93%	88%	75%	79%	nd	100%	100%
Spec 1	24%	45%	20%	24%	51%	20%	nd	51%	51%
Cutoff 2	1.15	1.19	1.15	1.15	1.15	0	nd	36.4	21.1
Sens 2	95%	83%	93%	88%	100%	100%	nd	100%	100%
Spec 2	24%	45%	20%	24%	18%	0%	nd	51%	51%
Cutoff 3	1.15	1.15	1.15	0	1.15	0	nd	36.4	21.1
Sens 3	95%	100%	93%	100%	100%	100%	nd	100%	100%
Spec 3	24%	18%	20%	0%	18%	0%	nd	51%	51%
Cutoff 4	189	295	189	189	295	189	nd	295	189
Sens 4	32%	33%	33%	41%	50%	42%	nd	50%	67%
Spec 4	70%	70%	71%	70%	70%	71%	nd	70%	71%
Cutoff 5	462	579	419	462	579	419	nd	579	419
Sens 5	21%	33%	20%	18%	25%	26%	nd	50%	67%
Spec 5	80%	81%	80%	80%	81%	80%	nd	81%	80%
Cutoff 6	1190	1230	1190	1190	1230	1190	nd	1230	1190
Sens 6	16%	17%	13%	12%	25%	16%	nd	50%	67%
Spec 6	90%	91%	91%	90%	91%	91%	nd	91%	91%
OR Quart 2	4.1	>4.6	12	1.8	>1.0	1.0	nd	>0	>1.1
p Value	0.076	<0.19	0.030	0.48	<0.98	1.0	nd	<na	<0.95
95% CI of	0.86	>0.47	1.3	0.35	>0.062	0.20	nd	>na	>0.061
OR Quart 2	20	na	120	9.2	na	5.0	nd	na	na
OR Quart 3	1.0	>0	3.5	1.8	>1.0	1.8	nd	>1.0	>0
p Value	1.0	<na	0.30	0.48	<0.98	0.45	nd	<0.97	<na
95% CI of	0.17	>na	0.32	0.35	>0.062	0.39	nd	>0.061	>na
OR Quart 3	5.8	na	38	9.2	na	8.2	nd	na	na
OR Quart 4	1.8	>2.1	5.1	1.3	>2.2	1.4	nd	>1.0	>2.4
p Value	0.48	<0.56	0.17	0.74	<0.53	0.69	nd	<1.0	<0.50
95% CI of	0.36	>0.18	0.50	0.25	>0.18	0.29	nd	>0.059	>0.19
OR Quart 4	9.1	na	52	7.2	na	6.4	nd	na	na

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	2300	3540	2300	2640	2300	2890
Average	2930	3880	2930	4210	2930	3140
Stdev	2240	4050	2240	6650	2240	1810
p (t-test)		7.5E−4		6.1E−4		0.55
Min	6.83	221	6.83	216	6.83	293
Max	22000	40700	22000	55700	22000	6560
n (Samp)	460	117	460	125	460	45
n (Patient)	223	117	223	125	223	45

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

sCr only						
Median	2840	2320	2840	2390	2840	1990
Average	3480	2560	3480	3160	3480	2390
Stdev	3360	1650	3360	2380	3360	1630
p (t-test)		0.087		0.52		0.11
Min	6.83	221	6.83	216	6.83	387
Max	55700	6210	55700	10800	55700	6110
n (Samp)	1008	39	1008	45	1008	25
n (Patient)	374	39	374	45	374	25
UO only						
Median	2410	3860	2410	3060	2410	2880
Average	3010	4670	3010	4630	3010	3260
Stdev	2070	4820	2070	7120	2070	1990
p (t-test)		9.0E−8		4.0E−5		0.44
Min	173	506	173	224	173	293
Max	11700	40700	11700	55700	11700	9700
n (Samp)	432	107	432	116	432	43
n (Patient)	172	107	172	116	172	43

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.61	0.40	0.66	0.56	0.46	0.58	0.56	0.37	0.56
SE	0.030	0.049	0.031	0.030	0.045	0.031	0.046	0.061	0.047
p	3.7E−4	0.044	6.1E−7	0.042	0.42	0.014	0.19	0.031	0.22
nCohort 1	460	1008	432	460	1008	432	460	1008	432
nCohort 2	117	39	107	125	45	116	45	25	43
Cutoff 1	2270	1090	2690	1950	1680	2040	2150	1190	2250
Sens 1	70%	72%	70%	70%	71%	71%	71%	72%	72%
Spec 1	50%	12%	55%	41%	25%	40%	47%	14%	45%
Cutoff 2	1550	994	2000	1250	1110	1560	1500	1110	1650
Sens 2	80%	82%	80%	80%	80%	80%	80%	80%	81%
Spec 2	30%	10%	39%	20%	13%	29%	28%	13%	31%
Cutoff 3	994	615	1450	898	883	986	485	491	881
Sens 3	91%	92%	91%	90%	91%	91%	91%	92%	91%
Spec 3	13%	4%	26%	10%	8%	12%	3%	2%	9%
Cutoff 4	3540	4070	3650	3540	4070	3650	3540	4070	3650
Sens 4	50%	18%	54%	37%	31%	39%	38%	16%	35%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	4180	4960	4430	4180	4960	4430	4180	4960	4430
Sens 5	31%	8%	33%	30%	20%	31%	31%	8%	26%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	5630	6470	6000	5630	6470	6000	5630	6470	6000
Sens 6	17%	0%	23%	20%	9%	20%	9%	0%	9%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.1	1.5	1.3	0.87	0.72	1.3	0.65	1.0	1.1
p Value	0.87	0.43	0.47	0.65	0.49	0.35	0.43	1.00	0.80
95% CI of	0.55	0.53	0.63	0.49	0.29	0.72	0.22	0.25	0.40
OR Quart 2	2.1	4.3	2.8	1.6	1.8	2.5	1.9	4.1	3.3
OR Quart 3	1.8	1.5	2.9	0.87	1.2	1.3	1.9	1.8	2.3
p Value	0.050	0.43	0.0021	0.65	0.67	0.43	0.15	0.36	0.083
95% CI of	1.00	0.53	1.5	0.49	0.53	0.69	0.80	0.51	0.90
OR Quart 3	3.4	4.3	5.7	1.6	2.7	2.4	4.5	6.1	5.8
OR Quart 4	2.6	2.6	3.7	1.7	1.2	2.1	1.6	2.6	1.9
p Value	0.0015	0.052	9.9E−5	0.048	0.67	0.015	0.29	0.11	0.17
95% CI of	1.4	0.99	1.9	1.0	0.53	1.2	0.67	0.80	0.75
OR Quart 4	4.7	6.8	7.3	3.0	2.7	3.7	3.9	8.3	5.1

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0285	0.0335	0.0285	0.0324	0.0285	0.0287
Average	2.78	1.92	2.78	2.63	2.78	1.54
Stdev	9.69	7.52	9.69	13.7	9.69	6.36
p (t-test)		0.37		0.89		0.39
Min	0.0110	0.0110	0.0110	0.0110	0.0110	0.0110
Max	92.3	63.9	92.3	134	92.3	41.7

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

n (Samp)	449	115	449	124	449	47
n (Patient)	222	115	222	124	222	47
sCr only						
Median	0.0285	0.0257	0.0285	0.0317	0.0285	0.0287
Average	2.84	0.930	2.84	1.03	2.84	2.16
Stdev	11.0	3.19	11.0	3.99	11.0	8.53
p (t-test)		0.30		0.27		0.76
Min	0.0110	0.0139	0.0110	0.0139	0.0110	0.0110
Max	159	13.9	159	24.4	159	41.7
n (Samp)	997	36	997	45	997	24
n (Patient)	379	36	379	45	379	24
UO only						
Median	0.0287	0.0335	0.0287	0.0312	0.0287	0.0287
Average	3.05	3.56	3.05	3.58	3.05	0.744
Stdev	10.6	13.1	10.6	17.5	10.6	2.23
p (t-test)		0.67		0.68		0.15
Min	0.0110	0.0110	0.0110	0.0110	0.0110	0.0139
Max	92.3	79.6	92.3	134	92.3	12.3
n (Samp)	419	107	419	115	419	44
n (Patient)	175	107	175	115	175	44

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.52	0.42	0.50	0.52	0.52	0.50	0.49	0.50	0.46
SE	0.030	0.051	0.031	0.030	0.044	0.030	0.045	0.060	0.047
p	0.58	0.11	0.97	0.49	0.68	0.99	0.80	0.99	0.45
nCohort 1	449	997	419	449	997	419	449	997	419
nCohort 2	115	36	107	124	45	115	47	24	44
Cutoff 1	0.0239	0.0217	0.0247	0.0237	0.0247	0.0239	0.0217	0.0239	0.0227
Sens 1	70%	72%	71%	73%	71%	70%	74%	71%	70%
Spec 1	38%	22%	40%	35%	41%	34%	27%	37%	26%
Cutoff 2	0.0205	0.0162	0.0159	0.0217	0.0217	0.0227	0.0205	0.0205	0.0205
Sens 2	80%	83%	86%	82%	82%	81%	83%	88%	84%
Spec 2	22%	15%	16%	27%	22%	26%	22%	18%	19%
Cutoff 3	0.0139	0.0110	0.0139	0.0147	0.0147	0.0147	0.0110	0.0139	0.0147
Sens 3	93%	100%	92%	91%	91%	90%	98%	92%	91%
Spec 3	8%	4%	7%	14%	11%	12%	4%	7%	12%
Cutoff 4	0.0526	0.0439	0.0526	0.0526	0.0439	0.0526	0.0526	0.0439	0.0526
Sens 4	16%	17%	17%	19%	18%	20%	19%	21%	18%
Spec 4	73%	73%	72%	73%	73%	72%	73%	73%	72%
Cutoff 5	1.17	0.327	1.42	1.17	0.327	1.42	1.17	0.327	1.42
Sens 5	14%	11%	15%	14%	13%	16%	13%	17%	11%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	6.80	6.49	8.01	6.80	6.49	8.01	6.80	6.49	8.01
Sens 6	9%	6%	7%	6%	4%	5%	4%	4%	2%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.0	1.3	2.7	1.7	0.62	1.8	2.3	0.66	2.5
p Value	1.0	0.58	0.0019	0.076	0.34	0.053	0.063	0.53	0.054
95% CI of	0.54	0.46	1.4	0.95	0.24	0.99	0.96	0.18	0.98
OR Quart 2	1.8	3.9	5.0	3.1	1.6	3.2	5.6	2.4	6.3
OR Quart 3	2.3	1.5	1.4	2.7	1.9	1.6	1.6	1.5	1.6
p Value	0.0030	0.43	0.31	7.0E−4	0.10	0.10	0.35	0.43	0.33
95% CI of	1.3	0.53	0.72	1.5	0.89	0.91	0.61	0.53	0.61
OR Quart 3	4.0	4.3	2.7	4.8	4.0	3.0	3.9	4.3	4.4
OR Quart 4	0.68	2.2	1.6	0.94	0.62	0.96	1.3	0.83	1.5
p Value	0.25	0.11	0.18	0.85	0.34	0.89	0.63	0.76	0.44
95% CI of	0.35	0.84	0.81	0.49	0.24	0.50	0.48	0.25	0.54
OR Quart 4	1.3	6.0	3.0	1.8	1.6	1.8	3.3	2.7	4.0

Myeloid differentiation primary response protein MyD88

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.000533	0.000171	0.000533	0.000533	0.000533	0.000165
Average	0.0182	0.0146	0.0182	0.0138	0.0182	0.000900
Stdev	0.0708	0.0619	0.0708	0.0330	0.0708	0.00127
p (t-test)		0.79		0.73		0.68
Min	0.000126	0.000126	0.000126	0.000126	0.000126	0.000165

TABLE 1-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Max	0.671	0.371	0.671	0.171	0.671	0.00237
n (Samp)	98	36	98	33	98	3
n (Patient)	64	36	64	33	64	3
sCr only						
Median	0.000533	0.000171	0.000533	0.000165	0.000533	0.000165
Average	0.0184	0.00598	0.0184	0.00792	0.0184	0.00225
Stdev	0.0636	0.0133	0.0636	0.0140	0.0636	0.00419
p (t-test)		0.52		0.59		0.61
Min	0.000126	0.000126	0.000126	0.000126	0.000126	0.000126
Max	0.671	0.0400	0.671	0.0359	0.671	0.00853
n (Samp)	192	11	192	11	192	4
n (Patient)	114	11	114	11	114	4
UO only						
Median	0.000533	0.000352	0.000533	0.000533	0.000533	0.000533
Average	0.0113	0.0169	0.0113	0.0134	0.0113	0.00485
Stdev	0.0229	0.0676	0.0229	0.0332	0.0229	0.0101
p (t-test)		0.48		0.68		0.50
Min	0.000126	0.000126	0.000126	0.000126	0.000126	0.000165
Max	0.106	0.371	0.106	0.171	0.106	0.0253
n (Samp)	99	30	99	34	99	6
n (Patient)	61	30	61	34	61	6

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.42	0.42	0.45	0.55	0.41	0.55	0.39	0.31	0.51
SE	0.057	0.092	0.061	0.059	0.093	0.058	0.18	0.15	0.12
p	0.17	0.41	0.39	0.37	0.31	0.37	0.54	0.21	0.92
nCohort 1	98	192	99	98	192	99	98	192	99
nCohort 2	36	11	30	33	11	34	3	4	6
Cutoff 1	0.000126	0.000126	0.000126	0.000171	0.000126	0.000171	0.000126	0.000126	0.000126
Sens 1	86%	91%	87%	73%	73%	74%	100%	75%	100%
Spec 1	8%	11%	9%	40%	11%	42%	8%	11%	9%
Cutoff 2	0.000126	0.000126	0.000126	0.000126	0	0.000126	0.000126	0	0.000126
Sens 2	86%	91%	87%	94%	100%	94%	100%	100%	100%
Spec 2	8%	11%	9%	8%	0%	9%	8%	0%	9%
Cutoff 3	0	0.000126	0	0.000126	0	0.000126	0.000126	0	0.000126
Sens 3	100%	91%	100%	94%	100%	94%	100%	100%	100%
Spec 3	0%	11%	0%	8%	0%	9%	8%	0%	9%
Cutoff 4	0.000533	0.00237	0.00309	0.000533	0.00237	0.00309	0.000533	0.00237	0.00309
Sens 4	22%	18%	27%	33%	27%	26%	33%	25%	17%
Spec 4	71%	70%	71%	71%	70%	71%	71%	70%	71%
Cutoff 5	0.0212	0.0190	0.0212	0.0212	0.0190	0.0212	0.0212	0.0190	0.0212
Sens 5	14%	18%	13%	18%	18%	18%	0%	0%	17%
Spec 5	81%	80%	81%	81%	80%	81%	81%	80%	81%
Cutoff 6	0.0484	0.0394	0.0393	0.0484	0.0394	0.0393	0.0484	0.0394	0.0393
Sens 6	3%	9%	3%	6%	0%	12%	0%	0%	0%
Spec 6	91%	90%	91%	91%	90%	91%	91%	90%	91%
OR Quart 2	0.12	0	1.3	3.0	0	3.2	>1.1	>1.0	1.0
p Value	0.055	na	0.71	0.048	na	0.055	<0.96	<0.99	1.0
95% CI of	0.014	na	0.37	1.0	na	0.98	>0.064	>0.062	0.13
OR Quart 2	1.0	na	4.3	8.8	na	10	na	na	7.7
OR Quart 3	3.4	3.9	0.64	0.23	1.4	2.1	>2.3	>2.1	0.48
p Value	0.024	0.10	0.53	0.083	0.70	0.23	<0.52	<0.55	0.56
95% CI of	1.2	0.77	0.16	0.044	0.29	0.62	>0.19	>0.18	0.041
OR Quart 3	10.0	20	2.5	1.2	6.4	7.1	na	na	5.6
OR Quart 4	2.2	1.0	3.1	1.3	1.4	1.7	>0	>1.0	0.46
p Value	0.16	0.98	0.051	0.61	0.68	0.39	<na	<0.99	0.54
95% CI of	0.74	0.14	0.99	0.43	0.30	0.50	>na	>0.062	0.039
OR Quart 4	6.6	7.5	9.5	4.2	6.6	5.9	na	na	5.4

TABLE 2

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Stromelysin-1:Metalloproteinase inhibitor 2 complex

	24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	0.487	0.487	nd	nd
Average	202	23.1	nd	nd
Stdev	1420	69.4	nd	nd
p (t-test)		0.63	nd	nd
Min	0.237	0.237	nd	nd
Max	13900	267	nd	nd
n (Samp)	97	15	nd	nd
n (Patient)	74	15	nd	nd
sCr only				
Median	0.487	10.9	nd	nd
Average	181	181	nd	nd
Stdev	1340	303	nd	nd
p (t-test)		1.00	nd	nd
Min	0.237	0.487	nd	nd
Max	13900	530	nd	nd
n (Samp)	110	3	nd	nd
n (Patient)	85	3	nd	nd
UO only				
Median	0.237	0.487	0.237	5.71
Average	217	24.0	217	5.71
Stdev	1550	72.0	1550	7.39
p (t-test)		0.64		0.85
Min	0.237	0.237	0.237	0.487
Max	13900	267	13900	10.9
n (Samp)	82	14	82	2
n (Patient)	62	14	62	2

	24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.63	0.80	0.63	nd	nd	0.77
SE	0.082	0.15	0.085	nd	nd	0.20
p	0.12	0.048	0.12	nd	nd	0.18
nCohort 1	97	110	82	nd	nd	82
nCohort 2	15	3	14	nd	nd	2
Cutoff 1	0.237	0.237	0.237	nd	nd	0.237
Sens 1	87%	100%	79%	nd	nd	100%
Spec 1	45%	44%	55%	nd	nd	55%
Cutoff 2	0.237	0.237	0	nd	nd	0.237
Sens 2	87%	100%	100%	nd	nd	100%
Spec 2	45%	44%	0%	nd	nd	55%
Cutoff 3	0	0.237	0	nd	nd	0.237
Sens 3	100%	100%	100%	nd	nd	100%
Spec 3	0%	44%	0%	nd	nd	55%
Cutoff 4	0.487	0.487	0.487	nd	nd	0.487
Sens 4	20%	67%	14%	nd	nd	50%
Spec 4	81%	82%	83%	nd	nd	83%
Cutoff 5	0.487	0.487	0.487	nd	nd	0.487
Sens 5	20%	67%	14%	nd	nd	50%
Spec 5	81%	82%	83%	nd	nd	83%
Cutoff 6	154	123	118	nd	nd	118
Sens 6	7%	33%	7%	nd	nd	0%
Spec 6	91%	90%	90%	nd	nd	90%
OR Quart 2	>21	>1.0	2.1	nd	nd	>0
p Value	<0.0051	<0.98	0.56	nd	nd	<na
95% CI of	>2.5	>0.062	0.18	nd	nd	>na
OR Quart 2	na	na	25	nd	nd	na
OR Quart 3	>0	>0	14	nd	nd	>1.0
p Value	<na	<na	0.018	nd	nd	<0.97
95% CI of	>na	>na	1.6	nd	nd	>0.061
OR Quart 3	na	na	120	nd	nd	na
OR Quart 4	>3.4	>2.1	2.1	nd	nd	>1.0
p Value	<0.31	<0.56	0.56	nd	nd	<0.97

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

95% CI of	>0.33	>0.18	0.18	nd	nd	>0.061
OR Quart 4	na	na	25	nd	nd	na

Heat shock 70 kDa protein 1

	24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	257	658	nd	nd
Average	500	1700	nd	nd
Stdev	872	3070	nd	nd
p (t-test)		0.0023	nd	nd
Min	0.297	0.335	nd	nd
Max	7800	11800	nd	nd
n (Samp)	95	14	nd	nd
n (Patient)	73	14	nd	nd
sCr only				
Median	283	1510	nd	nd
Average	534	1440	nd	nd
Stdev	897	318	nd	nd
p (t-test)		0.085	nd	nd
Min	0.297	1090	nd	nd
Max	7800	1710	nd	nd
n (Samp)	107	3	nd	nd
n (Patient)	83	3	nd	nd
UO only				
Median	225	435	225	1660
Average	503	1590	503	1660
Stdev	930	3220	930	215
p (t-test)		0.014		0.083
Min	0.297	0.335	0.297	1510
Max	7800	11800	7800	1820
n (Samp)	82	13	82	2
n (Patient)	62	13	62	2

	24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.70	0.93	0.62	nd	nd	0.96
SE	0.082	0.10	0.088	nd	nd	0.10
p	0.015	2.3E−5	0.17	nd	nd	5.5E−6
nCohort 1	95	107	82	nd	nd	82
nCohort 2	14	3	13	nd	nd	2
Cutoff 1	401	1040	246	nd	nd	1340
Sens 1	71%	100%	77%	nd	nd	100%
Spec 1	60%	91%	52%	nd	nd	94%
Cutoff 2	246	1040	125	nd	nd	1340
Sens 2	86%	100%	85%	nd	nd	100%
Spec 2	49%	91%	33%	nd	nd	94%
Cutoff 3	125	1040	23.5	nd	nd	1340
Sens 3	93%	100%	92%	nd	nd	100%
Spec 3	29%	91%	12%	nd	nd	94%
Cutoff 4	529	545	512	nd	nd	512
Sens 4	57%	100%	46%	nd	nd	100%
Spec 4	71%	70%	71%	nd	nd	71%
Cutoff 5	755	770	755	nd	nd	755
Sens 5	50%	100%	38%	nd	nd	100%
Spec 5	80%	80%	80%	nd	nd	80%
Cutoff 6	1020	1040	1020	nd	nd	1020
Sens 6	36%	100%	23%	nd	nd	100%
Spec 6	91%	91%	90%	nd	nd	90%
OR Quart 2	2.1	>0	0.95	nd	nd	>0
p Value	0.56	<na	0.96	nd	nd	<na
95% CI of	0.18	>na	0.12	nd	nd	>na
OR Quart 2	24	na	7.4	nd	nd	na
OR Quart 3	4.5	>0	2.1	nd	nd	>0
p Value	0.19	<na	0.42	nd	nd	<na
95% CI of	0.47	>na	0.35	nd	nd	>na
OR Quart 3	43	na	13	nd	nd	na
OR Quart 4	8.7	>3.2	2.8	nd	nd	>2.2

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

p Value	0.051	<0.32	0.26	nd	nd	<0.53
95% CI of	0.99	>0.32	0.48	nd	nd	>0.19
OR Quart 4	76	na	16	nd	nd	na

Insulin-like growth factor 1 receptor

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0103	0.0170	0.0103	0.0197	nd	nd
Average	0.0238	0.0170	0.0238	0.0407	nd	nd
Stdev	0.0708	0.0233	0.0708	0.0903	nd	nd
p (t-test)		0.89		0.41	nd	nd
Min	0.000123	0.000519	0.000123	0.00132	nd	nd
Max	0.679	0.0335	0.679	0.365	nd	nd
n (Samp)	95	2	95	15	nd	nd
n (Patient)	74	2	74	15	nd	nd
sCr only						
Median	nd	nd	0.0103	0.0197	nd	nd
Average	nd	nd	0.0263	0.0160	nd	nd
Stdev	nd	nd	0.0743	0.00637	nd	nd
p (t-test)	nd	nd		0.81	nd	nd
Min	nd	nd	0.000123	0.00862	nd	nd
Max	nd	nd	0.679	0.0197	nd	nd
n (Samp)	nd	nd	108	3	nd	nd
n (Patient)	nd	nd	85	3	nd	nd
UO only						
Median	nd	nd	0.0103	0.0150	0.0103	0.0261
Average	nd	nd	0.0248	0.0422	0.0248	0.0261
Stdev	nd	nd	0.0761	0.0935	0.0761	0.0247
p (t-test)	nd	nd		0.45		0.98
Min	nd	nd	0.000123	0.00132	0.000123	0.00862
Max	nd	nd	0.679	0.365	0.679	0.0436
n (Samp)	nd	nd	82	14	82	2
n (Patient)	nd	nd	64	14	64	2

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.51	nd	nd	0.62	0.57	0.62	nd	nd	0.65
SE	0.21	nd	nd	0.082	0.17	0.085	nd	nd	0.21
p	0.96	nd	nd	0.16	0.68	0.16	nd	nd	0.48
nCohort 1	95	nd	nd	95	108	82	nd	nd	82
nCohort 2	2	nd	nd	15	3	14	nd	nd	2
Cutoff 1	0.000172	nd	nd	0.00862	0.00573	0.00862	nd	nd	0.00454
Sens 1	100%	nd	nd	80%	100%	79%	nd	nd	100%
Spec 1	13%	nd	nd	40%	31%	44%	nd	nd	34%
Cutoff 2	0.000172	nd	nd	0.00862	0.00573	0.00454	nd	nd	0.00454
Sens 2	100%	nd	nd	80%	100%	86%	nd	nd	100%
Spec 2	13%	nd	nd	40%	31%	34%	nd	nd	34%
Cutoff 3	0.000172	nd	nd	0.00132	0.00573	0.00132	nd	nd	0.00454
Sens 3	100%	nd	nd	93%	100%	93%	nd	nd	100%
Spec 3	13%	nd	nd	27%	31%	32%	nd	nd	34%
Cutoff 4	0.0197	nd	nd	0.0197	0.0197	0.0197	nd	nd	0.0197
Sens 4	50%	nd	nd	40%	0%	43%	nd	nd	50%
Spec 4	73%	nd	nd	73%	70%	72%	nd	nd	72%
Cutoff 5	0.0292	nd	nd	0.0292	0.0292	0.0292	nd	nd	0.0292
Sens 5	50%	nd	nd	13%	0%	14%	nd	nd	50%
Spec 5	83%	nd	nd	83%	82%	83%	nd	nd	83%
Cutoff 6	0.0423	nd	nd	0.0423	0.0423	0.0423	nd	nd	0.0423
Sens 6	0%	nd	nd	7%	0%	7%	nd	nd	50%
Spec 6	92%	nd	nd	92%	91%	91%	nd	nd	91%
OR Quart 2	0	nd	nd	4.3	>1.0	>8.0	nd	nd	>1.0
p Value	na	nd	nd	0.20	<1.0	<0.064	nd	nd	<0.97
95% CI of	na	nd	nd	0.45	>0.059	>0.88	nd	nd	>0.061
OR Quart 2	na	nd	nd	42	na	na	nd	nd	na
OR Quart 3	0	nd	nd	5.9	>2.1	>3.4	nd	nd	>0
p Value	na	nd	nd	0.12	<0.56	<0.30	nd	nd	<na
95% CI of	na	nd	nd	0.64	>0.18	>0.33	nd	nd	>na
OR Quart 3	na	nd	nd	54	na	na	nd	nd	na

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

OR Quart 4	0.96	nd	nd	5.7	>0	>6.3	nd	nd	>1.0
p Value	0.98	nd	nd	0.13	<na	<0.11	nd	nd	<0.97
95% CI of	0.057	nd	nd	0.61	>na	>0.68	nd	nd	>0.061
OR Quart 4	16	nd	nd	52	na	na	nd	nd	na

Alpha-1-antitrypsin Neutrophil elastase complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	16.2	272	16.2	43.9	16.2	10.7
Average	65.3	222	65.3	168	65.3	39.0
Stdev	120	142	120	184	120	44.5
p (t-test)		0.013		0.011		0.57
Min	0.946	14.8	0.946	2.36	0.946	1.04
Max	400	329	400	400	400	97.9
n (Samp)	93	4	93	12	93	7
n (Patient)	67	4	67	12	67	7
sCr only						
Median	17.7	154	17.7	206	17.7	5.41
Average	73.1	154	73.1	206	73.1	136
Stdev	124	196	124	274	124	229
p (t-test)		0.37		0.14		0.40
Min	0.946	14.8	0.946	12.3	0.946	1.23
Max	400	292	400	400	400	400
n (Samp)	117	2	117	2	117	3
n (Patient)	83	2	83	2	83	3
UO only						
Median	17.3	252	17.3	55.1	17.3	38.5
Average	80.5	198	80.5	172	80.5	46.8
Stdev	137	165	137	176	137	43.7
p (t-test)		0.15		0.048		0.55
Min	1.27	12.7	1.27	2.36	1.27	1.04
Max	400	329	400	400	400	97.9
n (Samp)	80	3	80	11	80	6
n (Patient)	59	3	59	11	59	6

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.79	0.67	0.71	0.70	0.68	0.69	0.45	0.39	0.53
SE	0.14	0.21	0.17	0.088	0.21	0.093	0.12	0.18	0.12
p	0.032	0.43	0.22	0.024	0.38	0.043	0.64	0.54	0.80
nCohort 1	93	117	80	93	117	80	93	117	80
nCohort 2	4	2	3	12	2	11	7	3	6
Cutoff 1	245	14.5	12.7	18.0	12.2	20.3	5.27	1.04	10.4
Sens 1	75%	100%	100%	75%	100%	73%	71%	100%	83%
Spec 1	89%	44%	42%	55%	41%	59%	23%	2%	34%
Cutoff 2	14.5	14.5	12.7	16.2	12.2	18.0	1.04	1.04	10.4
Sens 2	100%	100%	100%	83%	100%	82%	86%	100%	83%
Spec 2	49%	44%	42%	51%	41%	52%	1%	2%	34%
Cutoff 3	14.5	14.5	12.7	12.2	12.2	16.2	0.946	1.04	0
Sens 3	100%	100%	100%	92%	100%	91%	100%	100%	100%
Spec 3	49%	44%	42%	45%	41%	48%	1%	2%	0%
Cutoff 4	31.8	42.5	31.9	31.8	42.5	31.9	31.8	42.5	31.9
Sens 4	75%	50%	67%	58%	50%	64%	43%	33%	50%
Spec 4	71%	70%	70%	71%	70%	70%	71%	70%	70%
Cutoff 5	57.4	76.0	76.0	57.4	76.0	76.0	57.4	76.0	76.0
Sens 5	75%	50%	67%	42%	50%	45%	43%	33%	33%
Spec 5	81%	80%	80%	81%	80%	80%	81%	80%	80%
Cutoff 6	347	347	400	347	347	400	347	347	400
Sens 6	0%	0%	0%	33%	50%	0%	0%	33%	0%
Spec 6	90%	91%	100%	90%	91%	100%	90%	91%	100%
OR Quart 2	>1.0	>1.0	>1.0	2.1	>1.0	2.0	0	0	2.0
p Value	<0.98	<1.0	<1.0	0.56	<1.0	0.58	na	na	0.58
95% CI of	>0.062	>0.060	>0.058	0.18	>0.060	0.17	na	na	0.17
OR Quart 2	na	na	na	25	na	24	na	na	24
OR Quart 3	>0	>0	>0	3.3	>0	3.1	0.31	0	0
p Value	<na	<na	<na	0.32	<na	0.34	0.32	na	na
95% CI of	>na	>na	>na	0.32	>na	0.30	0.030	na	na

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

OR Quart 3	na	na	na	34	na	33	3.2	na	na
OR Quart 4	>3.3	>1.0	>2.1	7.1	>1.0	5.8	1.0	2.1	3.2
p Value	<0.32	<1.0	<0.56	0.079	<1.0	0.12	1.0	0.56	0.34
95% CI of	>0.32	>0.060	>0.18	0.80	>0.060	0.62	0.18	0.18	0.30
OR Quart 4	na	na	na	64	na	55	5.5	24	33

Interstitial collagenase:Metalloproteinase inhibitor 2 complex

	24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	0.233	0.233		
Average	177	26.6		
Stdev	1620	76.2		
p (t-test)		0.72		
Min	0.228	0.228		
Max	16000	297		
n (Samp)	97	15		
n (Patient)	74	15		
sCr only				
Median	0.233	6.97		
Average	159	12.2		
Stdev	1530	15.3		
p (t-test)		0.87		
Min	0.228	0.233		
Max	16000	29.5		
n (Samp)	110	3		
n (Patient)	85	3		
UO only				
Median	0.233	0.233	0.233	0.231
Average	202	28.0	202	0.231
Stdev	1770	78.9	1770	0.00389
p (t-test)		0.71		0.87
Min	0.228	0.228	0.228	0.228
Max	16000	297	16000	0.233
n (Samp)	82	14	82	2
n (Patient)	62	14	62	2

	24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.55	0.78	0.51	nd	nd	0.34
SE	0.082	0.16	0.084	nd	nd	0.21
p	0.51	0.079	0.94	nd	nd	0.47
nCohort 1	97	110	82	nd	nd	82
nCohort 2	15	3	14	nd	nd	2
Cutoff 1	0	0.228	0	nd	nd	0
Sens 1	100%	100%	100%	nd	nd	100%
Spec 1	0%	37%	0%	nd	nd	0%
Cutoff 2	0	0.228	0	nd	nd	0
Sens 2	100%	100%	100%	nd	nd	100%
Spec 2	0%	37%	0%	nd	nd	0%
Cutoff 3	0	0.228	0	nd	nd	0
Sens 3	100%	100%	100%	nd	nd	100%
Spec 3	0%	37%	0%	nd	nd	0%
Cutoff 4	0.233	0.233	0.233	nd	nd	0.233
Sens 4	40%	67%	36%	nd	nd	0%
Spec 4	81%	79%	79%	nd	nd	79%
Cutoff 5	0.233	1.35	1.26	nd	nd	1.26
Sens 5	40%	67%	36%	nd	nd	0%
Spec 5	81%	80%	80%	nd	nd	80%
Cutoff 6	18.2	18.5	10.7	nd	nd	10.7
Sens 6	20%	33%	21%	nd	nd	0%
Spec 6	91%	91%	90%	nd	nd	90%
OR Quart 2	0.17	>0	1.0	nd	nd	>0
p Value	0.12	<na	1.0	nd	nd	<na
95% CI of	0.019	>na	0.22	nd	nd	>na
OR Quart 2	1.6	na	4.6	nd	nd	na
OR Quart 3	0.55	>1.0	0.22	nd	nd	>1.0
p Value	0.45	<0.98	0.19	nd	nd	<0.97

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

95% CI of	0.12	>0.062	0.022	nd	nd	>0.061
OR Quart 3	2.6	na	2.1	nd	nd	na
OR Quart 4	1.3	>2.1	1.3	nd	nd	>1.0
p Value	0.74	<0.56	0.71	nd	nd	<0.97
95% CI of	0.33	>0.18	0.31	nd	nd	>0.061
OR Quart 4	4.7	na	5.6	nd	nd	na

72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex

	24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	28.1	269	nd	nd
Average	585	1600	nd	nd
Stdev	1940	4100	nd	nd
p (t-test)		0.12	nd	nd
Min	1.15	1.15	nd	nd
Max	16000	16000	nd	nd
n (Samp)	91	15	nd	nd
n (Patient)	72	15	nd	nd
sCr only				
Median	30.3	527	nd	nd
Average	817	447	nd	nd
Stdev	2580	245	nd	nd
p (t-test)		0.81	nd	nd
Min	1.15	171	nd	nd
Max	16000	642	nd	nd
n (Samp)	105	3	nd	nd
n (Patient)	84	3	nd	nd
UO only				
Median	16.2	231	16.2	5640
Average	624	1660	624	5640
Stdev	2060	4240	2060	7740
p (t-test)		0.15		0.0023
Min	1.15	1.15	1.15	171
Max	16000	16000	16000	11100
n (Samp)	80	14	80	2
n (Patient)	63	14	63	2

	24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.60	0.75	0.57	nd	nd	0.83
SE	0.083	0.17	0.086	nd	nd	0.18
p	0.22	0.14	0.40	nd	nd	0.066
nCohort 1	91	105	80	nd	nd	80
nCohort 2	15	3	14	nd	nd	2
Cutoff 1	1.15	164	1.15	nd	nd	164
Sens 1	80%	100%	79%	nd	nd	100%
Spec 1	18%	65%	15%	nd	nd	68%
Cutoff 2	1.15	164	0	nd	nd	164
Sens 2	80%	100%	100%	nd	nd	100%
Spec 2	18%	65%	0%	nd	nd	68%
Cutoff 3	0	164	0	nd	nd	164
Sens 3	100%	100%	100%	nd	nd	100%
Spec 3	0%	65%	0%	nd	nd	68%
Cutoff 4	189	295	227	nd	nd	227
Sens 4	60%	67%	50%	nd	nd	50%
Spec 4	70%	70%	70%	nd	nd	70%
Cutoff 5	579	595	579	nd	nd	579
Sens 5	33%	33%	29%	nd	nd	50%
Spec 5	80%	80%	80%	nd	nd	80%
Cutoff 6	1380	1700	1380	nd	nd	1380
Sens 6	20%	0%	21%	nd	nd	50%
Spec 6	90%	90%	90%	nd	nd	90%
OR Quart 2	0.21	>0	0.61	nd	nd	>0
p Value	0.18	<na	0.60	nd	nd	<na
95% CI of	0.022	>na	0.092	nd	nd	>na
OR Quart 2	2.0	na	4.0	nd	nd	na
OR Quart 3	1.0	>1.0	1.4	nd	nd	>1.1

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

p Value	1.0	<0.98	0.68	nd	nd	<0.97
95% CI of	0.22	>0.062	0.28	nd	nd	>0.061
OR Quart 3	4.5	na	7.1	nd	nd	na
OR Quart 4	1.6	>2.2	1.8	nd	nd	>1.0
p Value	0.53	<0.54	0.48	nd	nd	<1.0
95% CI of	0.39	>0.18	0.37	nd	nd	>0.058
OR Quart 4	6.4	na	8.4	nd	nd	na

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	2660	3570	2660	2810	2660	2310
Average	3280	3960	3280	4330	3280	2870
Stdev	2980	2720	2980	6820	2980	2250
p (t-test)		0.087		0.014		0.39
Min	6.83	85.5	6.83	375	6.83	138
Max	48400	15000	48400	55700	48400	9700
n (Samp)	923	60	923	68	923	38
n (Patient)	359	60	359	68	359	38
sCr only						
Median	2820	2420	2820	2620	2820	2470
Average	3470	2380	3470	3790	3470	3290
Stdev	3270	1460	3270	2950	3270	2340
p (t-test)		0.20		0.68		0.83
Min	6.83	301	6.83	921	6.83	932
Max	55700	4670	55700	10800	55700	8410
n (Samp)	1219	15	1219	18	1219	16
n (Patient)	439	15	439	18	439	16
UO only						
Median	2740	4130	2740	3060	2740	2460
Average	3340	4790	3340	4830	3340	2990
Stdev	2980	4070	2980	7620	2980	2240
p (t-test)		6.9E−4		0.0014		0.50
Min	0.234	85.5	0.234	375	0.234	138
Max	48400	26600	48400	55700	48400	9700
n (Samp)	819	55	819	61	819	34
n (Patient)	285	55	285	61	285	34

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.59	0.39	0.64	0.54	0.52	0.55	0.44	0.48	0.46
SE	0.040	0.078	0.041	0.037	0.070	0.039	0.049	0.073	0.052
p	0.029	0.15	8.7E−4	0.30	0.73	0.24	0.24	0.83	0.41
nCohort 1	923	1219	819	923	1219	819	923	1219	819
nCohort 2	60	15	55	68	18	61	38	16	34
Cutoff 1	2430	1120	2720	2030	2080	2030	1250	1050	1650
Sens 1	70%	73%	71%	71%	72%	70%	71%	75%	71%
Spec 1	46%	14%	50%	36%	35%	34%	17%	12%	26%
Cutoff 2	1680	848	2290	1210	1700	1220	957	965	1180
Sens 2	80%	80%	80%	81%	83%	80%	82%	81%	82%
Spec 2	28%	8%	41%	16%	26%	15%	11%	10%	15%
Cutoff 3	873	615	1220	1040	1080	1040	402	950	402
Sens 3	90%	93%	91%	91%	94%	90%	92%	94%	91%
Spec 3	8%	4%	15%	13%	12%	11%	2%	10%	2%
Cutoff 4	3890	4060	3930	3890	4060	3930	3890	4060	3930
Sens 4	45%	7%	53%	38%	39%	41%	26%	38%	26%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	4730	4960	4750	4730	4960	4750	4730	4960	4750
Sens 5	35%	0%	44%	28%	28%	31%	21%	25%	21%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	6230	6520	6280	6230	6520	6280	6230	6520	6280
Sens 6	20%	0%	24%	16%	17%	18%	8%	6%	9%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.65	6.1	1.7	1.1	2.0	1.2	0.49	0.40	0.66
p Value	0.36	0.094	0.25	0.72	0.32	0.56	0.20	0.27	0.44
95% CI of	0.26	0.73	0.67	0.56	0.50	0.59	0.17	0.076	0.23
OR Quart 2	1.6	51	4.5	2.3	8.1	2.7	1.5	2.1	1.9

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

OR Quart 3	1.5	2.0	1.8	0.93	1.3	0.84	1.1	0.80	1.1
p Value	0.27	0.57	0.25	0.84	0.70	0.67	0.82	0.74	0.81
95% CI of	0.72	0.18	0.68	0.44	0.30	0.37	0.46	0.21	0.45
OR Quart 3	3.3	22	4.5	2.0	6.0	1.9	2.7	3.0	2.8
OR Quart 4	1.9	6.1	3.7	1.5	1.7	1.7	1.2	1.0	1.0
p Value	0.082	0.094	0.0029	0.24	0.48	0.16	0.66	1.00	0.99
95% CI of	0.92	0.73	1.6	0.76	0.40	0.82	0.52	0.29	0.39
OR Quart 4	3.9	51	8.8	3.0	7.1	3.4	2.9	3.5	2.6

Myeloid differentiation primary response protein MyD88

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.000533	0.000352	0.000533	0.000533	0.000533	0.00237
Average	0.0158	0.0168	0.0158	0.0123	0.0158	0.00355
Stdev	0.0587	0.0263	0.0587	0.0363	0.0587	0.00366
p (t-test)		0.96		0.78		0.64
Min	0.000126	0.000126	0.000126	0.000126	0.000126	0.000171
Max	0.671	0.0804	0.671	0.171	0.671	0.00853
n (Samp)	197	10	197	23	197	5
n (Patient)	118	10	118	23	118	5
sCr only						
Median	nd	nd	0.000533	0.000168	nd	nd
Average	nd	nd	0.0165	0.000259	nd	nd
Stdev	nd	nd	0.0575	0.000183	nd	nd
p (t-test)	nd	nd		0.57	nd	nd
Min	nd	nd	0.000126	0.000165	nd	nd
Max	nd	nd	0.671	0.000533	nd	nd
n (Samp)	nd	nd	239	4	nd	nd
n (Patient)	nd	nd	138	4	nd	nd
UO only						
Median	0.000533	0.000352	0.000533	0.000533	0.000533	0.00145
Average	0.0131	0.0168	0.0131	0.0128	0.0131	0.00305
Stdev	0.0363	0.0263	0.0363	0.0370	0.0363	0.00350
p (t-test)		0.75		0.97		0.50
Min	0.000126	0.000126	0.000126	0.000126	0.000126	0.000171
Max	0.371	0.0804	0.371	0.171	0.371	0.00853
n (Samp)	181	10	181	22	181	6
n (Patient)	105	10	105	22	105	6

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.54	nd	0.53	0.46	0.34	0.46	0.62	nd	0.60
SE	0.095	nd	0.096	0.065	0.15	0.066	0.14	nd	0.12
p	0.71	nd	0.74	0.49	0.28	0.56	0.36	nd	0.42
nCohort 1	197	nd	181	197	239	181	197	nd	181
nCohort 2	10	nd	10	23	4	22	5	nd	6
Cutoff 1	0.000165	nd	0.000165	0.000126	0.000126	0.000126	0.000171	nd	0.000171
Sens 1	80%	nd	80%	91%	100%	91%	80%	nd	83%
Spec 1	35%	nd	33%	10%	10%	10%	42%	nd	41%
Cutoff 2	0.000165	nd	0.000165	0.000126	0.000126	0.000126	0.000171	nd	0.000171
Sens 2	80%	nd	80%	91%	100%	91%	80%	nd	83%
Spec 2	35%	nd	33%	10%	10%	10%	42%	nd	41%
Cutoff 3	0	nd	0	0.000126	0.000126	0.000126	0.000165	nd	0.000165
Sens 3	100%	nd	100%	91%	100%	91%	100%	nd	100%
Spec 3	0%	nd	0%	10%	10%	10%	35%	nd	33%
Cutoff 4	0.00167	nd	0.00309	0.00167	0.00309	0.00309	0.00167	nd	0.00309
Sens 4	40%	nd	40%	22%	0%	23%	60%	nd	33%
Spec 4	70%	nd	70%	70%	70%	70%	70%	nd	70%
Cutoff 5	0.0184	nd	0.0188	0.0184	0.0188	0.0188	0.0184	nd	0.0188
Sens 5	40%	nd	40%	17%	0%	18%	0%	nd	0%
Spec 5	80%	nd	80%	80%	80%	80%	80%	nd	80%
Cutoff 6	0.0387	nd	0.0366	0.0387	0.0393	0.0366	0.0387	nd	0.0366
Sens 6	10%	nd	10%	9%	0%	9%	0%	nd	0%
Spec 6	90%	nd	90%	90%	90%	90%	90%	nd	90%
OR Quart 2	2.0	nd	1.5	0	>1.0	0.38	>1.0	nd	>3.1
p Value	0.42	nd	0.67	na	<0.99	0.26	<1.0	nd	<0.33
95% CI of	0.36	nd	0.24	na	>0.062	0.069	>0.061	nd	>0.31

TABLE 2-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

OR Quart 2	12	nd	9.4	na	na	2.0	na	nd	na
OR Quart 3	0	nd	0.48	3.1	>3.2	1.2	>3.2	nd	>3.1
p Value	na	nd	0.55	0.046	<0.33	0.75	<0.32	nd	<0.33
95% CI of	na	nd	0.042	1.0	>0.32	0.35	>0.32	nd	>0.31
OR Quart 3	na	nd	5.5	9.4	na	4.3	na	nd	na
OR Quart 4	2.0	nd	2.0	1.0	>0	2.0	>1.0	nd	>0
p Value	0.42	nd	0.42	1.0	<na	0.24	<1.0	nd	<na
95% CI of	0.36	nd	0.36	0.27	>na	0.63	>0.061	nd	>na
OR Quart 4	12	nd	12	3.7	na	6.5	na	nd	na

TABLE 3

Comparison of marker levels in urine samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F). Tumor necrosis factor ligand superfamily member 10

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0287	0.0287	0.0257	0.0285	0.0335	0.0286
Average	1.65	2.49	0.779	0.732	2.34	2.49
Stdev	7.15	8.75	2.82	1.39	8.97	9.35
p (t-test)		0.53		0.96		0.93
Min	0.0110	0.0110	0.0139	0.0139	0.0110	0.0110
Max	63.9	50.6	13.9	3.82	63.9	50.6
n (Samp)	121	43	47	11	99	30
n (Patient)	121	43	47	11	99	30

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.53	0.59	0.49
SE	0.052	0.099	0.061
p	0.61	0.36	0.88
nCohort 1	121	47	99
nCohort 2	43	11	30
Cutoff 1	0.0239	0.0237	0.0239
Sens 1	77%	73%	73%
Spec 1	35%	47%	32%
Cutoff 2	0.0227	0.0227	0.0227

TABLE 3-continued

Comparison of marker levels in urine samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F). Tumor necrosis factor ligand superfamily member 10

Sens 2	84%	82%	83%
Spec 2	30%	38%	28%
Cutoff 3	0.0159	0.0139	0.0159
Sens 3	91%	91%	90%
Spec 3	15%	6%	15%
Cutoff 4	0.0439	0.0363	0.0439
Sens 4	26%	36%	20%
Spec 4	73%	74%	73%
Cutoff 5	0.0526	0.0439	0.0526
Sens 5	21%	36%	17%
Spec 5	85%	81%	84%
Cutoff 6	1.70	2.23	1.70
Sens 6	16%	18%	17%
Spec 6	90%	91%	91%
OR Quart 2	2.8	0.92	1.3
p Value	0.050	0.94	0.71
95% CI of	1.00	0.11	0.37
OR Quart 2	7.9	7.6	4.3
OR Quart 3	1.6	1.6	3.1
p Value	0.42	0.62	0.051
95% CI of	0.53	0.23	0.99
OR Quart 3	4.6	12	9.5
OR Quart 4	1.8	2.2	0.64
p Value	0.29	0.42	0.53
95% CI of	0.61	0.33	0.16
OR Quart 4	5.2	14	2.5

TABLE 4

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Stromelysin-1:Metalloproteinase inhibitor 2 complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.487	0.487	0.487	0.487	0.487	0.487
Average	400	101	400	101	400	0.487
Stdev	2140	197	2140	197	2140	0
p (t-test)		0.70		0.70		0.75
Min	0.237	0.487	0.237	0.487	0.237	0.487
Max	13900	530	13900	530	13900	0.487
n (Samp)	42	8	42	8	42	3
n (Patient)	42	8	42	8	42	3

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

sCr only						
Median	0.487	5.71	0.487	5.71	nd	nd
Average	238	136	238	136	nd	nd
Stdev	1630	263	1630	263	nd	nd
p (t-test)		0.90		0.90	nd	nd
Min	0.237	0.487	0.237	0.487	nd	nd
Max	13900	530	13900	530	nd	nd
n (Samp)	73	4	73	4	nd	nd
n (Patient)	73	4	73	4	nd	nd
UO only						
Median	0.487	0.487	0.487	0.487	0.487	0.487
Average	435	53.8	435	53.8	435	0.487
Stdev	2350	119	2350	119	2350	0
p (t-test)		0.72		0.72		0.75
Min	0.237	0.487	0.237	0.487	0.237	0.487
Max	13900	267	13900	267	13900	0.487
n (Samp)	35	5	35	5	35	3
n (Patient)	35	5	35	5	35	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.68	0.76	0.69	0.68	0.76	0.69	0.56	nd	0.63
SE	0.11	0.14	0.14	0.11	0.14	0.14	0.18	nd	0.18
p	0.11	0.076	0.17	0.11	0.076	0.17	0.74	nd	0.48
nCohort 1	42	73	35	42	73	35	42	nd	35
nCohort 2	8	4	5	8	4	5	3	nd	3
Cutoff 1	0.237	0.237	0.237	0.237	0.237	0.237	0.237	nd	0.237
Sens 1	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 1	31%	42%	46%	31%	42%	46%	31%	nd	46%
Cutoff 2	0.237	0.237	0.237	0.237	0.237	0.237	0.237	nd	0.237
Sens 2	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 2	31%	42%	46%	31%	42%	46%	31%	nd	46%
Cutoff 3	0.237	0.237	0.237	0.237	0.237	0.237	0.237	nd	0.237
Sens 3	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 3	31%	42%	46%	31%	42%	46%	31%	nd	46%
Cutoff 4	0.487	0.487	0.487	0.487	0.487	0.487	0.487	nd	0.487
Sens 4	38%	50%	20%	38%	50%	20%	0%	nd	0%
Spec 4	81%	82%	80%	81%	82%	80%	81%	nd	80%
Cutoff 5	0.487	0.487	0.487	0.487	0.487	0.487	0.487	nd	0.487
Sens 5	38%	50%	20%	38%	50%	20%	0%	nd	0%
Spec 5	81%	82%	80%	81%	82%	80%	81%	nd	80%
Cutoff 6	261	154	201	261	154	201	261	nd	201
Sens 6	25%	25%	20%	25%	25%	20%	0%	nd	0%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	>7.5	>2.2	>6.7	>7.5	>2.2	>6.7	>4.1	nd	>3.9
p Value	<0.090	<0.53	<0.12	<0.090	<0.53	<0.12	<0.25	nd	<0.28
95% CI of	>0.73	>0.19	>0.60	>0.73	>0.19	>0.60	>0.36	nd	>0.33
OR Quart 2	na	na	na	na	na	na	na	nd	na
OR Quart 3	>0	>0	>0	>0	>0	>0	>0	nd	>0
p Value	<na	<na	<na	<na	<na	<na	<na	nd	<na
95% CI of	>na	>na	>na	>na	>na	>na	>na	nd	>na
OR Quart 3	na	na	na	na	na	na	na	nd	na
OR Quart 4	>3.6	>2.1	>1.1	>3.6	>2.1	>1.1	>0	nd	>0
p Value	<0.30	<0.56	<0.94	<0.30	<0.56	<0.94	<na	nd	<na
95% CI of	>0.32	>0.18	>0.060	>0.32	>0.18	>0.060	>na	nd	>na
OR Quart4	na	na	na	na	na	na	na	nd	na

Heat shock 70 kDa protein 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	338	1320	338	1320	338	1320
Average	633	2600	633	2600	633	4450
Stdev	1230	4080	1230	4080	1230	6370
p (t-test)		0.013		0.013		0.0012
Min	0.297	250	0.297	250	0.297	250

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Max	7800	11800	7800	11800	7800	11800
n (Samp)	41	7	41	7	41	3
n (Patient)	41	7	41	7	41	3
sCr only						
Median	408	1300	408	1300	nd	nd
Average	620	1140	620	1140	nd	nd
Stdev	1040	648	1040	648	nd	nd
p (t-test)		0.33		0.33	nd	nd
Min	0.297	250	0.297	250	nd	nd
Max	7800	1710	7800	1710	nd	nd
n (Samp)	71	4	71	4	nd	nd
n (Patient)	71	4	71	4	nd	nd
UO only						
Median	277	934	277	934	277	1320
Average	664	3480	664	3480	664	4450
Stdev	1330	5560	1330	5560	1330	6370
p (t-test)		0.013		0.013		0.0031
Min	0.297	250	0.297	250	0.297	250
Max	7800	11800	7800	11800	7800	11800
n (Samp)	35	4	35	4	35	3
n (Patient)	35	4	35	4	35	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.83	0.80	0.75	0.83	0.80	0.75	0.79	nd	0.79
SE	0.099	0.14	0.15	0.099	0.14	0.15	0.16	nd	0.16
p	8.2E−4	0.027	0.084	8.2E−4	0.027	0.084	0.066	nd	0.077
nCohort 1	41	71	35	41	71	35	41	nd	35
nCohort 2	7	4	4	7	4	4	3	nd	3
Cutoff 1	1020	1040	512	1020	1040	512	245	nd	225
Sens 1	71%	75%	75%	71%	75%	75%	100%	nd	100%
Spec 1	88%	90%	66%	88%	90%	66%	46%	nd	49%
Cutoff 2	512	245	225	512	245	225	245	nd	225
Sens 2	86%	100%	100%	86%	100%	100%	100%	nd	100%
Spec 2	66%	41%	49%	66%	41%	49%	46%	nd	49%
Cutoff 3	245	245	225	245	245	225	245	nd	225
Sens 3	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 3	46%	41%	49%	46%	41%	49%	46%	nd	49%
Cutoff 4	596	627	596	596	627	596	596	nd	596
Sens 4	71%	75%	50%	71%	75%	50%	67%	nd	67%
Spec 4	71%	70%	71%	71%	70%	71%	71%	nd	71%
Cutoff 5	811	812	755	811	812	755	811	nd	755
Sens 5	71%	75%	50%	71%	75%	50%	67%	nd	67%
Spec 5	80%	80%	80%	80%	80%	80%	80%	nd	80%
Cutoff 6	1150	1040	1340	1150	1040	1340	1150	nd	1340
Sens 6	57%	75%	25%	57%	75%	25%	67%	nd	33%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	>1.1	>1.0	>1.0	>1.1	>1.0	>1.0	>1.1	nd	>1.0
p Value	<0.95	<1.0	<1.0	<0.95	<1.0	<1.0	<0.95	nd	<1.0
95% CI of	>0.061	>0.058	>0.054	>0.061	>0.058	>0.054	>0.060	nd	>0.054
OR Quart 2	na	na	na	na	na	na	na	nd	na
OR Quart 3	>1.1	>0	>1.0	>1.1	>0	>1.0	>0	nd	>0
p Value	<0.95	<na	<1.0	<0.95	<na	<1.0	<na	nd	<na
95% CI of	>0.061	>na	>0.054	>0.061	>na	>0.054	>na	nd	>na
OR Quart 3	na	na	na	na	na	na	na	nd	na
OR Quart 4	>8.6	>3.4	>2.2	>8.6	>3.4	>2.2	>2.4	nd	>2.2
p Value	<0.072	<0.31	<0.54	<0.072	<0.31	<0.54	<0.49	nd	<0.54
95% CI of	>0.83	>0.32	>0.17	>0.83	>0.32	>0.17	>0.19	nd	>0.17
OR Quart 4	na	na	na	na	na	na	na	nd	na

Interstitial collagenase:Metalloproteinase inhibitor 2 complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.233	6.57	0.233	6.57	0.233	0.228
Average	396	48.1	396	48.1	396	2.21

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Stdev	2470	102	2470	102	2470	3.43
p (t-test)		0.69		0.69		0.79
Min	0.228	0.228	0.228	0.228	0.228	0.228
Max	16000	297	16000	297	16000	6.17
n (Samp)	42	8	42	8	42	3
n (Patient)	42	8	42	8	42	3
sCr only						
Median	0.233	6.57	0.233	6.57	nd	nd
Average	233	10.7	233	10.7	nd	nd
Stdev	1870	12.9	1870	12.9	nd	nd
p (t-test)		0.81		0.81	nd	nd
Min	0.228	0.233	0.228	0.233	nd	nd
Max	16000	29.5	16000	29.5	nd	nd
n (Samp)	73	4	73	4	nd	nd
n (Patient)	73	4	73	4	nd	nd
UO only						
Median	0.233	6.17	0.233	6.17	0.233	0.228
Average	462	69.6	462	69.6	462	2.21
Stdev	2700	129	2700	129	2700	3.43
p (t-test)		0.75		0.75		0.77
Min	0.228	0.228	0.228	0.228	0.228	0.228
Max	16000	297	16000	297	16000	6.17
n (Samp)	35	5	35	5	35	3
n (Patient)	35	5	35	5	35	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.68	0.77	0.59	0.68	0.77	0.59	0.41	nd	0.35
SE	0.11	0.14	0.14	0.11	0.14	0.14	0.18	nd	0.18
p	0.12	0.055	0.51	0.12	0.055	0.51	0.63	nd	0.41
nCohort 1	42	73	35	42	73	35	42	nd	35
nCohort 2	8	4	5	8	4	5	3	nd	3
Cutoff 1	0.228	5.57	0	0.228	5.57	0	0	nd	0
Sens 1	75%	75%	100%	75%	75%	100%	100%	nd	100%
Spec 1	45%	79%	0%	45%	79%	0%	0%	nd	0%
Cutoff 2	0	0.228	0	0	0.228	0	0	nd	0
Sens 2	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 2	0%	36%	0%	0%	36%	0%	0%	nd	0%
Cutoff 3	0	0.228	0	0	0.228	0	0	nd	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 3	0%	36%	0%	0%	36%	0%	0%	nd	0%
Cutoff 4	0.233	0.233	0.233	0.233	0.233	0.233	0.233	nd	0.233
Sens 4	62%	75%	60%	62%	75%	60%	33%	nd	33%
Spec 4	76%	75%	71%	76%	75%	71%	76%	nd	71%
Cutoff 5	6.97	6.17	7.29	6.97	6.17	7.29	6.97	nd	7.29
Sens 5	38%	50%	40%	38%	50%	40%	0%	nd	0%
Spec 5	81%	82%	80%	81%	82%	80%	81%	nd	80%
Cutoff 6	30.3	30.3	18.5	30.3	30.3	18.5	30.3	nd	18.5
Sens 6	25%	0%	40%	25%	0%	40%	0%	nd	0%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0	>0	0	0	>0	0	0	nd	0
p Value	na	<na	na	na	<na	na	na	nd	na
95% CI of	na	>na	na	na	>na	na	na	nd	na
OR Quart 2	na	na	na	na	na	na	na	nd	na
OR Quart 3	1.0	>1.1	0.44	1.0	>1.1	0.44	0	nd	0
p Value	1.0	<0.97	0.54	1.0	<0.97	0.54	na	nd	na
95% CI of	0.12	>0.061	0.034	0.12	>0.061	0.034	na	nd	na
OR Quart 3	8.6	na	5.9	8.6	na	5.9	na	nd	na
OR Quart 4	2.2	>3.4	1.0	2.2	>3.4	1.0	2.4	nd	2.6
p Value	0.42	<0.31	1.0	0.42	<0.31	1.0	0.49	nd	0.48
95% CI of	0.33	>0.32	0.11	0.33	>0.32	0.11	0.19	nd	0.19
OR Quart 4	15	na	8.9	15	na	8.9	32	nd	34

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	117	411	117	411	117	269
Average	756	2460	756	2460	756	685
Stdev	2540	5500	2540	5500	2540	961
p (t-test)		0.17		0.17		0.96
Min	1.15	1.15	1.15	1.15	1.15	1.15
Max	16000	16000	16000	16000	16000	1780
n (Samp)	40	8	40	8	40	3
n (Patient)	40	8	40	8	40	3
sCr only						
Median	110	398	110	398	nd	nd
Average	889	402	889	402	nd	nd
Stdev	2800	219	2800	219	nd	nd
p (t-test)		0.73		0.73	nd	nd
Min	1.15	171	1.15	171	nd	nd
Max	16000	642	16000	642	nd	nd
n (Samp)	72	4	72	4	nd	nd
n (Patient)	72	4	72	4	nd	nd
UO only						
Median	57.4	295	57.4	295	57.4	269
Average	772	3670	772	3670	772	685
Stdev	2710	6930	2710	6930	2710	961
p (t-test)		0.083		0.083		0.96
Min	1.15	1.15	1.15	1.15	1.15	1.15
Max	16000	16000	16000	16000	16000	1780
n (Samp)	35	5	35	5	35	3
n (Patient)	35	5	35	5	35	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.68	0.69	0.68	0.68	0.69	0.68	0.56	nd	0.57
SE	0.11	0.15	0.14	0.11	0.15	0.14	0.18	nd	0.18
p	0.099	0.21	0.21	0.099	0.21	0.21	0.73	nd	0.69
nCohort 1	40	72	35	40	72	35	40	nd	35
nCohort 2	8	4	5	8	4	5	3	nd	3
Cutoff 1	234	234	234	234	234	234	0	nd	0
Sens 1	75%	75%	80%	75%	75%	80%	100%	nd	100%
Spec 1	68%	64%	69%	68%	64%	69%	0%	nd	0%
Cutoff 2	164	164	234	164	164	234	0	nd	0
Sens 2	88%	100%	80%	88%	100%	80%	100%	nd	100%
Spec 2	57%	57%	69%	57%	57%	69%	0%	nd	0%
Cutoff 3	0	164	0	0	164	0	0	nd	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 3	0%	57%	0%	0%	57%	0%	0%	nd	0%
Cutoff 4	398	419	398	398	419	398	398	nd	398
Sens 4	50%	50%	40%	50%	50%	40%	33%	nd	33%
Spec 4	70%	71%	71%	70%	71%	71%	70%	nd	71%
Cutoff 5	615	656	579	615	656	579	615	nd	579
Sens 5	38%	0%	40%	38%	0%	40%	33%	nd	33%
Spec 5	80%	81%	80%	80%	81%	80%	80%	nd	80%
Cutoff 6	1230	1380	1230	1230	1380	1230	1230	nd	1230
Sens 6	25%	0%	40%	25%	0%	40%	33%	nd	33%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0	>0	0	0	>0	0	0	nd	0
p Value	na	<na	na	na	<na	na	na	nd	na
95% CI of	na	>na	na	na	>na	na	na	nd	na
OR Quart 2	na	na	na	na	na	na	na	nd	na
OR Quart 3	5.5	>3.6	2.2	5.5	>3.6	2.2	0.90	nd	1.0
p Value	0.16	<0.29	0.54	0.16	<0.29	0.54	0.94	nd	1.0
95% CI of	0.51	>0.34	0.17	0.51	>0.34	0.17	0.049	nd	0.053
OR Quart 3	59	na	30	59	na	30	17	nd	19
OR Quart 4	3.7	>1.1	2.2	3.7	>1.1	2.2	0.90	nd	0.89
p Value	0.29	<0.97	0.54	0.29	<0.97	0.54	0.94	nd	0.94

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

95% CI of	0.32	>0.061	0.17	0.32	>0.061	0.17	0.049	nd	0.047
OR Quart 4	42	na	30	42	na	30	17	nd	17

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	2820	4940	2820	4490	2820	3900
Average	3370	6950	3370	6450	3370	4660
Stdev	2580	9680	2580	9690	2580	2330
p (t-test)		1.0E−5		1.4E−4		0.053
Min	6.83	171	6.83	171	6.83	1650
Max	22000	55700	22000	55700	22000	9700
n (Samp)	223	30	223	30	223	16
n (Patient)	223	30	223	30	223	16
sCr only						
Median	3740	4080	3740	4080	3740	5050
Average	4470	4560	4470	4510	4470	5290
Stdev	4470	2180	4470	2210	4470	1870
p (t-test)		0.95		0.97		0.63
Min	6.83	171	6.83	171	6.83	3280
Max	55700	7860	55700	7860	55700	7860
n (Samp)	374	13	374	13	374	7
n (Patient)	374	13	374	13	374	7
UO only						
Median	3220	5250	3220	5050	3220	4490
Average	3650	8910	3650	8250	3650	4750
Stdev	2320	11500	2320	11500	2320	2360
p (t-test)		2.8E−7		6.5E−6		0.090
Min	485	1700	485	1120	485	1650
Max	11700	55700	11700	55700	11700	9700
n (Samp)	172	23	172	23	172	14
n (Patient)	172	23	172	23	172	14

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.73	0.58	0.75	0.68	0.57	0.69	0.69	0.67	0.65
SE	0.054	0.084	0.061	0.056	0.084	0.064	0.076	0.11	0.082
p	1.9E−5	0.34	3.2E−5	0.0016	0.38	0.0035	0.013	0.13	0.074
nCohort 1	223	374	172	223	374	172	223	374	172
nCohort 2	30	13	23	30	13	23	16	7	14
Cutoff 1	3720	3410	3960	3110	3250	3110	3250	3970	3280
Sens 1	70%	77%	74%	70%	77%	74%	75%	71%	71%
Spec 1	65%	46%	65%	57%	44%	49%	59%	56%	52%
Cutoff 2	3250	3250	3280	2440	2870	2460	3110	3720	2690
Sens 2	80%	85%	83%	80%	85%	83%	81%	86%	86%
Spec 2	59%	44%	52%	43%	37%	39%	57%	50%	43%
Cutoff 3	2210	2200	2690	1740	2200	1740	1700	3250	1700
Sens 3	90%	92%	91%	90%	92%	91%	94%	100%	93%
Spec 3	41%	27%	43%	27%	27%	22%	26%	44%	21%
Cutoff 4	3940	5270	4360	3940	5270	4360	3940	5270	4360
Sens 4	63%	31%	65%	57%	31%	61%	50%	29%	50%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	4960	6450	5580	4960	6450	5580	4960	6450	5580
Sens 5	50%	23%	48%	47%	23%	43%	38%	29%	36%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	6160	7760	6670	6160	7760	6670	6160	7760	6670
Sens 6	33%	15%	35%	30%	15%	35%	25%	29%	21%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.5	4.1	4.2	2.1	4.1	1.3	2.0	>2.0	0.98
p Value	0.65	0.21	0.21	0.31	0.21	0.72	0.58	<0.56	0.98
95% CI of	0.25	0.45	0.45	0.50	0.45	0.28	0.18	>0.18	0.13
OR Quart 2	9.5	37	39	8.8	37	6.3	23	na	7.3
OR Quart 3	5.1	5.2	7.8	2.1	5.2	2.1	6.4	>3.1	2.7
p Value	0.043	0.14	0.059	0.31	0.14	0.32	0.089	<0.33	0.25
95% CI of	1.1	0.59	0.93	0.50	0.59	0.49	0.75	>0.32	0.49

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

OR Quart 3	25	45	66	8.8	45	8.9	55	na	15
OR Quart 4	10	3.0	14	6.1	3.0	3.8	7.7	>2.0	2.6
p Value	0.0027	0.34	0.014	0.0061	0.34	0.052	0.061	<0.57	0.27
95% CI of	2.2	0.31	1.7	1.7	0.31	0.99	0.91	>0.18	0.48
OR Quart 4	46	30	110	22	30	15	64	na	14

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0363	0.348	0.0363	0.338	0.0363	0.336
Average	4.58	11.4	4.58	10.8	4.58	1.86
Stdev	13.0	31.2	13.0	31.3	13.0	2.64
p (t-test)		0.032		0.048		0.40
Min	0.0110	0.0159	0.0110	0.0159	0.0110	0.0159
Max	92.3	134	92.3	134	92.3	8.63
n (Samp)	222	30	222	30	222	16
n (Patient)	222	30	222	30	222	16
sCr only						
Median	0.0410	0.0597	0.0410	0.0410	0.0410	0.636
Average	5.75	2.45	5.75	2.45	5.75	2.67
Stdev	16.4	3.54	16.4	3.54	16.4	3.52
p (t-test)		0.47		0.47		0.62
Min	0.0110	0.0159	0.0110	0.0159	0.0110	0.0159
Max	159	9.58	159	9.58	159	8.63
n (Samp)	379	13	379	13	379	7
n (Patient)	379	13	379	13	379	7
UO only						
Median	0.0439	1.51	0.0439	0.670	0.0439	0.336
Average	5.67	17.5	5.67	13.4	5.67	1.74
Stdev	15.3	37.7	15.3	35.4	15.3	2.70
p (t-test)		0.0059		0.064		0.34
Min	0.0110	0.0217	0.0110	0.0217	0.0110	0.0239
Max	92.3	134	92.3	134	92.3	9.58
n (Samp)	175	23	175	23	175	14
n (Patient)	175	23	175	23	175	14

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.63	0.55	0.63	0.61	0.52	0.61	0.59	0.56	0.56
SE	0.057	0.084	0.066	0.058	0.082	0.066	0.077	0.11	0.082
p	0.020	0.51	0.050	0.047	0.84	0.10	0.24	0.60	0.49
nCohort 1	222	379	175	222	379	175	222	379	175
nCohort 2	30	13	23	30	13	23	16	7	14
Cutoff 1	0.0335	0.0257	0.0335	0.0285	0.0239	0.0335	0.0285	0.0392	0.0335
Sens 1	70%	77%	74%	70%	85%	74%	75%	71%	71%
Spec 1	48%	31%	39%	41%	27%	39%	41%	49%	39%
Cutoff 2	0.0257	0.0239	0.0285	0.0239	0.0239	0.0285	0.0247	0.0217	0.0247
Sens 2	80%	85%	83%	80%	85%	83%	81%	86%	86%
Spec 2	39%	27%	34%	39%	27%	34%	39%	20%	30%
Cutoff 3	0.0239	0.0217	0.0239	0.0239	0.0217	0.0239	0.0237	0.0147	0.0239
Sens 3	90%	92%	91%	90%	92%	91%	94%	100%	93%
Spec 3	38%	20%	30%	38%	20%	30%	38%	8%	30%
Cutoff 4	0.775	1.53	1.42	0.775	1.53	1.42	0.775	1.53	1.42
Sens 4	47%	38%	52%	47%	38%	43%	44%	43%	36%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	4.08	5.16	4.69	4.08	5.16	4.69	4.08	5.16	4.69
Sens 5	27%	23%	30%	23%	23%	22%	12%	29%	7%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	11.8	16.4	15.0	11.8	16.4	15.0	11.8	16.4	15.0
Sens 6	13%	0%	22%	10%	0%	13%	0%	0%	0%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	12	1.5	4.5	6.5	2.0	4.5	4.1	0	>8.2
p Value	0.021	0.65	0.067	0.019	0.42	0.067	0.21	na	<0.053
95% CI of	1.4	0.25	0.90	1.4	0.37	0.90	0.45	na	>0.97
OR Quart 2	94	9.3	22	30	11	22	38	na	na

TABLE 4-continued

Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

OR Quart 3	7.8	2.0	2.1	3.2	1.5	3.3	5.4	1.5	>3.2
p Value	0.059	0.42	0.41	0.16	0.65	0.16	0.13	0.65	<0.32
95% CI of	0.92	0.37	0.36	0.62	0.25	0.63	0.61	0.25	>0.32
OR Quart 3	65	11	12	17	9.3	17	47	9.3	na
OR Quart 4	15	2.0	5.2	6.5	2.0	3.8	6.4	0.99	>4.3
p Value	0.011	0.42	0.043	0.019	0.42	0.11	0.089	0.99	<0.20
95% CI of	1.8	0.37	1.1	1.4	0.37	0.75	0.75	0.14	>0.46
OR Quart 4	120	11	25	30	11	19	55	7.2	na

TABLE 5

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Heat shock 70 kDa protein 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	641	1370	641	1200	641	2350
Average	1400	2760	1400	1990	1400	2240
Stdev	2010	3320	2010	2130	2010	2100
p (t-test)		0.057		0.25		0.26
Min	0.288	0.288	0.288	128	0.288	54.3
Max	10000	10700	10000	9450	10000	6660
n (Samp)	54	14	54	24	54	9
n (Patient)	53	14	53	24	53	9
sCr only						
Median	840	1950	840	1240	840	1720
Average	1580	2450	1580	1240	1580	1470
Stdev	2190	1690	2190	1030	2190	1030
p (t-test)		0.50		0.83		0.93
Min	0.288	1070	0.288	514	0.288	340
Max	10700	4330	10700	1970	10700	2350
n (Samp)	111	3	111	2	111	3
n (Patient)	93	3	93	2	93	3
UO only						
Median	641	1370	641	1220	641	963
Average	1390	2740	1390	2040	1390	2010
Stdev	1860	3550	1860	2110	1860	2200
p (t-test)		0.073		0.18		0.38
Min	0.288	0.288	0.288	128	0.288	54.3
Max	10000	10700	10000	9450	10000	6660
n (Samp)	48	12	48	25	48	9
n (Patient)	44	12	44	25	44	9

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.61	0.75	0.58	0.66	0.59	0.66	0.65	0.62	0.59
SE	0.088	0.17	0.095	0.070	0.21	0.070	0.11	0.18	0.11
p	0.21	0.13	0.43	0.023	0.69	0.025	0.16	0.49	0.39
nCohort 1	54	111	48	54	111	48	54	111	48
nCohort 2	14	3	12	24	2	25	9	3	9
Cutoff 1	705	1000	387	837	507	837	500	336	310
Sens 1	71%	100%	75%	71%	100%	72%	78%	100%	78%
Spec 1	54%	56%	42%	56%	41%	54%	44%	31%	38%
Cutoff 2	0.288	1000	0.288	514	507	664	310	336	248
Sens 2	86%	100%	83%	83%	100%	80%	89%	100%	89%
Spec 2	4%	56%	4%	46%	41%	52%	37%	31%	29%
Cutoff 3	0	1000	0	310	507	310	48.9	336	48.9
Sens 3	100%	100%	100%	92%	100%	92%	100%	100%	100%
Spec 3	0%	56%	0%	37%	41%	38%	11%	31%	12%
Cutoff 4	1370	1500	1500	1370	1500	1500	1370	1500	1500
Sens 4	50%	67%	42%	46%	50%	48%	56%	67%	44%

TABLE 5-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Spec 4	70%	70%	71%	70%	70%	71%	70%	70%	71%
Cutoff 5	2700	2550	2700	2700	2550	2700	2700	2550	2700
Sens 5	36%	33%	33%	21%	0%	24%	33%	0%	33%
Spec 5	81%	80%	81%	81%	80%	81%	81%	80%	81%
Cutoff 6	3540	3540	3630	3540	3540	3630	3540	3540	3630
Sens 6	29%	33%	25%	12%	0%	12%	11%	0%	11%
Spec 6	91%	90%	92%	91%	90%	92%	91%	90%	92%
OR Quart 2	0.62	>0	0.62	3.6	>1.0	5.1	2.0	>1.0	3.5
p Value	0.63	<na	0.63	0.15	<0.98	0.068	0.59	<1.0	0.30
95% CI of	0.090	>na	0.087	0.63	>0.062	0.89	0.16	>0.060	0.32
OR Quart 2	4.3	na	4.3	21	na	29	25	na	39
OR Quart 3	1.0	>1.0	1.0	5.0	>0	6.4	0.93	>0	1.0
p Value	1.0	<0.98	1.0	0.071	<na	0.036	0.96	<na	1.0
95% CI of	0.17	>0.062	0.17	0.87	>na	1.1	0.053	>na	0.056
OR Quart 3	5.8	na	6.0	28	na	36	16	na	18
OR Quart 4	2.5	>2.1	1.5	7.0	>1.0	5.8	6.4	>2.1	4.7
p Value	0.25	<0.56	0.67	0.026	<1.0	0.046	0.11	<0.56	0.19
95% CI of	0.52	>0.18	0.26	1.3	>0.060	1.0	0.65	>0.18	0.46
OR Quart 4	13	na	8.0	38	na	33	63	na	49

Insulin-like growth factor 1 receptor

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0498	0.0502	0.0498	0.0556	0.0498	0.0331
Average	0.207	0.622	0.207	0.470	0.207	0.899
Stdev	0.797	3.22	0.797	2.43	0.797	4.04
p (t-test)		0.28		0.38		0.15
Min	9.84E−5	0.000208	9.84E−5	0.000211	9.84E−5	0.000208
Max	6.23	18.2	6.23	14.8	6.23	19.4
n (Samp)	79	32	79	37	79	23
n (Patient)	70	32	70	37	70	23
sCr only						
Median	0.0498	0.0255	0.0498	0.0595	0.0498	0.0398
Average	0.124	2.30	0.124	1.92	0.124	2.20
Stdev	0.523	6.44	0.523	5.22	0.523	6.46
p (t-test)		1.0E−5		1.4E−5		2.5E−5
Min	9.84E−5	0.000208	9.84E−5	0.000211	9.84E−5	0.0214
Max	6.23	18.2	6.23	14.8	6.23	19.4
n (Samp)	187	8	187	8	187	9
n (Patient)	126	8	126	8	126	9
UO only						
Median	0.0498	0.0572	0.0498	0.0556	0.0498	0.0354
Average	0.233	0.808	0.233	0.589	0.233	0.0641
Stdev	0.851	3.96	0.851	3.27	0.851	0.126
p (t-test)		0.25		0.39		0.42
Min	0.000208	0.000208	0.000208	0.000211	0.000208	0.000208
Max	6.23	21.0	6.23	20.5	6.23	0.543
n (Samp)	69	28	69	39	69	17
n (Patient)	57	28	57	39	57	17

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.48	0.34	0.51	0.55	0.50	0.55	0.40	0.49	0.38
SE	0.061	0.11	0.065	0.058	0.10	0.058	0.070	0.099	0.080
p	0.72	0.14	0.82	0.37	0.98	0.35	0.17	0.93	0.14
nCohort 1	79	187	69	79	187	69	79	187	69
nCohort 2	32	8	28	37	8	39	23	9	17
Cutoff 1	0.0219	0.0137	0.0398	0.0373	0.00497	0.0373	0.0212	0.0283	0.0212
Sens 1	72%	75%	71%	73%	75%	74%	83%	78%	76%
Spec 1	28%	14%	46%	43%	9%	43%	24%	28%	23%
Cutoff 2	0.0178	0.000208	0.0212	0.0251	0.000211	0.0325	0.0212	0.0219	0.000224
Sens 2	81%	88%	82%	81%	88%	82%	83%	89%	82%
Spec 2	20%	3%	23%	28%	5%	39%	24%	23%	7%
Cutoff 3	0.0134	0.000172	0.0134	0.00497	0.000208	0.0178	0.000208	0.0212	0.000208
Sens 3	91%	100%	93%	92%	100%	92%	96%	100%	94%
Spec 3	16%	1%	14%	10%	3%	22%	3%	18%	3%
Cutoff 4	0.0839	0.0729	0.0839	0.0839	0.0729	0.0839	0.0839	0.0729	0.0839

TABLE 5-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Sens 4	16%	12%	21%	27%	25%	26%	9%	33%	6%
Spec 4	73%	70%	72%	73%	70%	72%	73%	70%	72%
Cutoff 5	0.0986	0.0876	0.101	0.0986	0.0876	0.101	0.0986	0.0876	0.101
Sens 5	12%	12%	14%	24%	25%	21%	9%	22%	6%
Spec 5	81%	80%	81%	81%	80%	81%	81%	80%	81%
Cutoff 6	0.135	0.133	0.176	0.135	0.133	0.176	0.135	0.133	0.176
Sens 6	12%	12%	7%	14%	25%	5%	9%	11%	6%
Spec 6	91%	90%	91%	91%	90%	91%	91%	90%	91%
OR Quart 2	2.0	1.0	1.0	1.4	0	2.1	3.8	0.49	8.4
p Value	0.24	1.0	1.0	0.56	na	0.24	0.13	0.57	0.060
95% CI of	0.62	0.061	0.27	0.44	na	0.62	0.69	0.043	0.91
OR Quart 2	6.7	16	3.7	4.5	na	6.8	21	5.6	77
OR Quart 3	1.5	2.0	2.1	1.9	0.98	3.2	6.4	2.1	6.2
p Value	0.54	0.57	0.22	0.26	0.98	0.050	0.028	0.41	0.11
95% CI of	0.43	0.18	0.63	0.62	0.19	1.00	1.2	0.36	0.66
OR Quart 3	5.0	23	7.3	6.0	5.1	11	33	12	58
OR Quart 4	1.5	4.4	0.95	1.7	0.64	2.1	3.8	1.0	6.6
p Value	0.49	0.20	0.94	0.39	0.63	0.24	0.13	1.0	0.10
95% CI of	0.45	0.47	0.26	0.53	0.10	0.62	0.69	0.14	0.70
OR Quart 4	5.2	41	3.5	5.2	4.0	6.8	21	7.4	62

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	183000	192000	183000	180000	183000	172000
Average	191000	193000	191000	185000	191000	179000
Stdev	79300	67000	79300	78800	79300	59800
p (t-test)		0.83		0.64		0.48
Min	1370	63300	1370	190	1370	49200
Max	520000	371000	520000	506000	520000	297000
n (Samp)	122	52	122	55	122	25
n (Patient)	88	52	88	55	88	25
sCr only						
Median	181000	199000	181000	210000	181000	179000
Average	184000	200000	184000	227000	184000	180000
Stdev	70200	62800	70200	97800	70200	54800
p (t-test)		0.38		0.030		0.87
Min	190	118000	190	129000	190	108000
Max	520000	316000	520000	506000	520000	280000
n (Samp)	291	16	291	14	291	9
n (Patient)	164	16	164	14	164	9
UO only						
Median	180000	182000	180000	180000	180000	172000
Average	189000	187000	189000	176000	189000	178000
Stdev	81700	69000	81700	63300	81700	59400
p (t-test)		0.92		0.32		0.57
Min	1080	63300	1080	190	1080	49200
Max	520000	371000	520000	337000	520000	297000
n (Samp)	124	43	124	57	124	23
n (Patient)	81	43	81	57	81	23

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.53	0.58	0.50	0.48	0.64	0.48	0.48	0.49	0.49
SE	0.048	0.077	0.051	0.047	0.082	0.047	0.064	0.099	0.066
p	0.59	0.30	0.98	0.72	0.098	0.63	0.71	0.90	0.84
nCohort 1	122	291	124	122	291	124	122	291	124
nCohort 2	52	16	43	55	14	57	25	9	23
Cutoff 1	152000	160000	141000	151000	175000	144000	147000	144000	147000
Sens 1	71%	75%	72%	71%	71%	70%	72%	78%	74%
Spec 1	32%	37%	23%	32%	46%	25%	27%	26%	28%
Cutoff 2	134000	125000	130000	133000	164000	123000	125000	115000	125000
Sens 2	81%	81%	81%	80%	86%	81%	80%	89%	83%
Spec 2	20%	17%	19%	20%	39%	12%	14%	14%	15%
Cutoff 3	106000	118000	105000	107000	133000	107000	115000	107000	115000
Sens 3	90%	94%	91%	91%	93%	91%	92%	100%	91%
Spec 3	9%	14%	9%	10%	21%	10%	11%	11%	12%

TABLE 5-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Cutoff 4	212000	207000	209000	212000	207000	209000	212000	207000	209000
Sens 4	31%	44%	33%	29%	50%	25%	32%	22%	35%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	227000	227000	228000	227000	227000	228000	227000	227000	228000
Sens 5	25%	38%	21%	25%	43%	23%	32%	22%	35%
Spec 5	80%	80%	81%	80%	80%	81%	80%	80%	81%
Cutoff 6	262000	262000	257000	262000	262000	257000	262000	262000	257000
Sens 6	13%	12%	14%	7%	14%	9%	8%	11%	9%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.87	0.48	0.66	0.75	2.1	1.1	0.32	1.0	0.21
p Value	0.76	0.41	0.41	0.53	0.41	0.77	0.11	1.0	0.058
95% CI of	0.34	0.085	0.24	0.30	0.37	0.47	0.078	0.14	0.041
OR Quart 2	2.2	2.7	1.8	1.9	12	2.8	1.3	7.3	1.1
OR Quart 3	0.89	0.99	0.86	0.75	1.0	0.74	0.85	1.5	0.85
p Value	0.81	0.98	0.75	0.53	1.0	0.52	0.77	0.65	0.77
95% CI of	0.35	0.24	0.33	0.30	0.14	0.29	0.27	0.25	0.27
OR Quart 3	2.3	4.1	2.2	1.9	7.3	1.9	2.6	9.4	2.6
OR Quart 4	1.2	1.5	0.86	1.1	3.1	1.4	0.88	1.0	0.72
p Value	0.70	0.53	0.75	0.76	0.17	0.46	0.82	1.0	0.59
95% CI of	0.48	0.41	0.33	0.48	0.61	0.58	0.28	0.14	0.22
OR Quart 4	2.9	5.6	2.2	2.7	16	3.3	2.7	7.3	2.3

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0228	0.0313	0.0228	0.0239	0.0228	0.0313
Average	8.36	2.81	8.36	4.03	8.36	6.36
Stdev	43.2	6.38	43.2	9.01	43.2	14.2
p (t-test)		0.40		0.54		0.85
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	31.9	292	35.0	292	44.8
n (Samp)	95	43	95	39	95	17
n (Patient)	69	43	69	39	69	17
sCr only						
Median	0.0313	0.0315	0.0313	0.0228	0.0313	4.67
Average	6.23	2.84	6.23	5.61	6.23	13.8
Stdev	29.8	9.15	29.8	11.2	29.8	18.7
p (t-test)		0.70		0.93		0.45
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	31.9	292	35.0	292	44.8
n (Samp)	223	12	223	18	223	9
n (Patient)	138	12	138	18	138	9
UO only						
Median	0.0313	0.0313	0.0313	0.0313	0.0313	0.0313
Average	9.24	2.29	9.24	4.53	9.24	0.671
Stdev	42.8	4.74	42.8	16.5	42.8	2.10
p (t-test)		0.32		0.51		0.46
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	16.7	292	98.4	292	7.88
n (Samp)	98	38	98	39	98	14
n (Patient)	67	38	67	39	67	14

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.51	0.49	0.47	0.52	0.44	0.47	0.65	0.70	0.49
SE	0.053	0.086	0.056	0.055	0.073	0.055	0.077	0.099	0.083
p	0.82	0.90	0.54	0.69	0.41	0.55	0.051	0.043	0.94
nCohort 1	95	223	98	95	223	98	95	223	98
nCohort 2	43	12	38	39	18	39	17	9	14
Cutoff 1	0.0162	0.0205	0.0197	0.0197	0.0162	0.0197	0.0247	0.0313	0.0269
Sens 1	81%	75%	71%	79%	83%	77%	88%	78%	79%
Spec 1	15%	24%	21%	25%	13%	21%	53%	54%	47%
Cutoff 2	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162	0.0247	0.0205	0.0197
Sens 2	81%	83%	82%	85%	83%	82%	88%	89%	86%
Spec 2	15%	13%	10%	15%	13%	10%	53%	24%	21%
Cutoff 3	0	0	0	0	0	0	0.0162	0	0.0162
Sens 3	100%	100%	100%	100%	100%	100%	94%	100%	93%

TABLE 5-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Spec 3	0%	0%	0%	0%	0%	0%	15%	0%	10%
Cutoff 4	0.0317	0.171	0.0363	0.0317	0.171	0.0363	0.0317	0.171	0.0363
Sens 4	30%	25%	26%	28%	22%	26%	41%	56%	14%
Spec 4	73%	70%	71%	73%	70%	71%	73%	70%	71%
Cutoff 5	0.328	3.32	1.53	0.328	3.32	1.53	0.328	3.32	1.53
Sens 5	30%	8%	21%	28%	22%	21%	35%	56%	7%
Spec 5	80%	80%	81%	80%	80%	81%	80%	80%	81%
Cutoff 6	4.64	10.8	7.32	4.64	10.8	7.32	4.64	10.8	7.32
Sens 6	19%	8%	16%	21%	22%	10%	29%	33%	7%
Spec 6	91%	90%	91%	91%	90%	91%	91%	90%	91%
OR Quart 2	0.54	2.1	0.85	1.1	0.75	0.90	1.6	1.0	2.2
p Value	0.26	0.41	0.78	0.85	0.71	0.85	0.64	1.0	0.40
95% CI of	0.19	0.36	0.28	0.38	0.16	0.31	0.24	0.061	0.36
OR Quart 2	1.6	12	2.6	3.2	3.5	2.6	10	16	13
OR Quart 3	0.76	1.5	0.85	1.0	1.3	0.77	2.8	2.0	3.5
p Value	0.60	0.65	0.78	1.0	0.71	0.63	0.24	0.57	0.14
95% CI of	0.28	0.25	0.28	0.34	0.33	0.26	0.50	0.18	0.65
OR Quart 3	2.1	9.5	2.6	3.0	5.1	2.3	16	23	19
OR Quart 4	1.1	1.6	1.7	1.3	1.6	1.4	4.3	5.4	1.0
p Value	0.87	0.64	0.30	0.65	0.49	0.55	0.086	0.13	1.0
95% CI of	0.41	0.25	0.61	0.45	0.42	0.49	0.81	0.61	0.13
OR Quart 4	2.9	9.7	4.8	3.6	5.9	3.8	23	48	7.6

Myeloid differentiation primary response protein MyD88

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.000368	0.000245	0.000368	0.000368	0.000368	0.000457
Average	0.00255	0.00199	0.00255	0.000350	0.00255	0.00458
Stdev	0.0181	0.00785	0.0181	9.42E−5	0.0181	0.0138
p (t-test)		0.86		0.46		0.72
Min	0.000224	0.000224	0.000224	0.000224	0.000224	0.000224
Max	0.171	0.0441	0.171	0.000457	0.171	0.0463
n (Samp)	90	33	90	37	90	11
n (Patient)	63	33	63	37	63	11
sCr only						
Median	0.000368	0.000245	0.000368	0.000224	0.000368	0.000457
Average	0.00184	0.000291	0.00184	0.000301	0.00184	0.000368
Stdev	0.0129	8.43E−5	0.0129	0.000121	0.0129	0.000122
p (t-test)		0.72		0.77		0.80
Min	0.000126	0.000224	0.000126	0.000224	0.000126	0.000224
Max	0.171	0.000457	0.171	0.000457	0.171	0.000457
n (Samp)	202	9	202	6	202	5
n (Patient)	121	9	121	6	121	5
UO only						
Median	0.000332	0.000245	0.000332	0.000368	0.000332	0.000457
Average	0.00450	0.00230	0.00450	0.000348	0.00450	0.00456
Stdev	0.0265	0.00850	0.0265	9.37E−5	0.0265	0.0138
p (t-test)		0.67		0.34		0.99
Min	0.000224	0.000224	0.000224	0.000224	0.000224	0.000224
Max	0.194	0.0441	0.194	0.000457	0.194	0.0463
n (Samp)	94	28	94	38	94	11
n (Patient)	58	28	58	38	58	11

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.42	0.40	0.45	0.53	0.36	0.55	0.71	0.60	0.68
SE	0.059	0.10	0.063	0.057	0.12	0.056	0.091	0.14	0.093
p	0.17	0.35	0.44	0.63	0.26	0.34	0.022	0.47	0.053
nCohort 1	90	202	94	90	202	94	90	202	94
nCohort 2	33	9	28	37	6	38	11	5	11
Cutoff 1	0	0.000224	0	0.000224	0.000126	0.000224	0.000296	0.000224	0.000296
Sens 1	100%	78%	100%	81%	100%	84%	91%	80%	82%
Spec 1	0%	24%	0%	21%	0%	24%	43%	24%	50%
Cutoff 2	0	0.000126	0	0.000224	0.000126	0.000224	0.000296	0.000224	0.000296
Sens 2	100%	100%	100%	81%	100%	84%	91%	80%	82%
Spec 2	0%	0%	0%	21%	0%	24%	43%	24%	50%
Cutoff 3	0	0.000126	0	0	0.000126	0	0.000296	0.000126	0.000224

TABLE 5-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Sens 3	100%	100%	100%	100%	100%	100%	91%	100%	91%
Spec 3	0%	0%	0%	0%	0%	0%	43%	0%	24%
Cutoff 4	0.000368	0.000368	0.000368	0.000368	0.000368	0.000368	0.000368	0.000368	0.000368
Sens 4	18%	11%	18%	32%	33%	32%	64%	60%	55%
Spec 4	71%	72%	72%	71%	72%	72%	71%	72%	72%
Cutoff 5	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457
Sens 5	6%	0%	7%	0%	0%	0%	9%	0%	9%
Spec 5	96%	96%	95%	96%	96%	95%	96%	96%	95%
Cutoff 6	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457	0.000457
Sens 6	6%	0%	7%	0%	0%	0%	9%	0%	9%
Spec 6	96%	96%	95%	96%	96%	95%	96%	96%	95%
OR Quart 2	1.5	0	1.9	1.5	0	1.2	0	0.98	1.0
p Value	0.52	na	0.32	0.46	na	0.78	na	0.99	1.0
95% CI of	0.42	na	0.54	0.51	na	0.39	na	0.060	0.059
OR Quart 2	5.4	na	6.6	4.5	na	3.5	na	16	17
OR Quart 3	2.5	6.6	1.8	1.3	0	1.6	11	0.98	3.3
p Value	0.14	0.085	0.35	0.63	na	0.42	0.029	0.99	0.32
95% CI of	0.73	0.77	0.52	0.44	na	0.53	1.3	0.060	0.32
OR Quart 3	8.4	57	6.3	3.9	na	4.6	99	16	34
OR Quart 4	3.0	2.1	1.6	0.96	2.1	1.4	2.0	2.0	7.1
p Value	0.075	0.55	0.48	0.94	0.41	0.58	0.58	0.58	0.079
95% CI of	0.90	0.18	0.44	0.31	0.36	0.46	0.17	0.18	0.80
OR Quart 4	10	24	5.7	3.0	12	4.0	24	23	64

TABLE 6

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Heat shock 70 kDa protein 1

	24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	934	840	934	928
Average	1680	957	1680	967
Stdev	2210	694	2210	860
p (t-test)		0.33		0.44
Min	0.288	16.7	0.288	0.288
Max	10700	2280	10700	1970
n (Samp)	113	9	113	6
n (Patient)	92	9	92	6
UO only				
Median	934	840	934	336
Average	1650	957	1650	817
Stdev	2190	694	2190	870
p (t-test)		0.35		0.40
Min	0.288	16.7	0.288	0.288
Max	10700	2280	10700	1970
n (Samp)	99	9	99	5
n (Patient)	77	9	77	5

	24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	0.47	0.44	nd	0.39
SE	0.10	nd	0.10	0.12	nd	0.14
p	0.73	nd	0.75	0.66	nd	0.44
nCohort 1	113	nd	99	113	nd	99
nCohort 2	9	nd	9	6	nd	5
Cutoff 1	705	nd	664	252	nd	252
Sens 1	78%	nd	78%	83%	nd	80%
Spec 1	44%	nd	44%	23%	nd	25%
Cutoff 2	114	nd	114	252	nd	252
Sens 2	89%	nd	89%	83%	nd	80%
Spec 2	15%	nd	16%	23%	nd	25%

TABLE 6-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Cutoff 3	4.58	nd	4.58	0	nd	0
Sens 3	100%	nd	100%	100%	nd	100%
Spec 3	6%	nd	7%	0%	nd	0%
Cutoff 4	1620	nd	1610	1620	nd	1610
Sens 4	11%	nd	11%	33%	nd	20%
Spec 4	71%	nd	71%	71%	nd	71%
Cutoff 5	2930	nd	2930	2930	nd	2930
Sens 5	0%	nd	0%	0%	nd	0%
Spec 5	81%	nd	81%	81%	nd	81%
Cutoff 6	3970	nd	4330	3970	nd	4330
Sens 6	0%	nd	0%	0%	nd	0%
Spec 6	90%	nd	91%	90%	nd	91%
OR Quart 2	3.3	nd	3.2	2.1	nd	>2.2
p Value	0.31	nd	0.32	0.56	nd	<0.54
95% CI of	0.33	nd	0.32	0.18	nd	>0.18
OR Quart 2	34	nd	33	24	nd	na
OR Quart 3	3.2	nd	3.2	1.0	nd	>2.2
p Value	0.32	nd	0.32	1.0	nd	<0.54
95% CI of	0.32	nd	0.32	0.060	nd	>0.18
OR Quart 3	33	nd	33	17	nd	na
OR Quart 4	2.1	nd	2.1	2.1	nd	>1.0
p Value	0.54	nd	0.56	0.54	nd	<0.98
95% CI of	0.18	nd	0.18	0.18	nd	>0.062
OR Quart 4	25	nd	24	25	nd	na

Insulin-like growth factor 1 receptor

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0484	0.0572	0.0484	0.0619	0.0484	0.0426
Average	0.346	2.67	0.346	0.938	0.346	1.38
Stdev	2.22	6.87	2.22	3.58	2.22	5.00
p (t-test)		0.017		0.32		0.13
Min	9.84E−5	0.0144	9.84E−5	0.000211	9.84E−5	0.000211
Max	21.0	18.2	21.0	14.8	21.0	19.4
n (Samp)	183	7	183	17	183	15
n (Patient)	122	7	122	17	122	15
sCr only						
Median	0.0498	0.0888	0.0498	7.45	0.0498	0.0596
Average	0.300	6.12	0.300	7.45	0.300	4.90
Stdev	2.01	10.5	2.01	10.4	2.01	9.70
p (t-test)		1.2E−5		3.9E−6		9.6E−5
Min	9.84E−5	0.0144	9.84E−5	0.0742	9.84E−5	0.0214
Max	21.0	18.2	21.0	14.8	21.0	19.4
n (Samp)	222	3	222	2	222	4
n (Patient)	145	3	145	2	145	4
UO only						
Median	0.0498	0.0572	0.0498	0.0572	0.0498	0.0449
Average	0.393	0.0892	0.393	0.0668	0.393	0.102
Stdev	2.37	0.0767	2.37	0.0525	2.37	0.149
p (t-test)		0.80		0.57		0.67
Min	0.000208	0.0390	0.000208	0.000211	0.000208	0.000211
Max	21.0	0.204	21.0	0.192	21.0	0.543
n (Samp)	159	4	159	17	159	12
n (Patient)	102	4	102	17	102	12

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.65	0.65	0.62	0.60	0.85	0.54	0.54	0.59	0.52
SE	0.11	0.17	0.15	0.075	0.17	0.075	0.079	0.15	0.088
p	0.19	0.38	0.42	0.17	0.038	0.61	0.58	0.55	0.80
nCohort 1	183	222	159	183	222	159	183	222	159
nCohort 2	7	3	4	17	2	17	15	4	12
Cutoff 1	0.0556	0.0137	0.0556	0.0407	0.0729	0.0373	0.0219	0.0390	0.0219
Sens 1	71%	100%	75%	71%	100%	71%	73%	75%	75%
Spec 1	60%	15%	57%	44%	72%	40%	25%	41%	23%
Cutoff 2	0.0373	0.0137	0.0373	0.0297	0.0729	0.0253	0.0212	0.0212	0.0212

TABLE 6-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Sens 2	86%	100%	100%	82%	100%	82%	93%	100%	92%
Spec 2	42%	15%	40%	33%	72%	25%	21%	20%	18%
Cutoff 3	0.0137	0.0137	0.0373	0.00949	0.0729	0.00497	0.0212	0.0212	0.0212
Sens 3	100%	100%	100%	94%	100%	94%	93%	100%	92%
Spec 3	15%	15%	40%	11%	72%	9%	21%	20%	18%
Cutoff 4	0.0692	0.0699	0.0729	0.0692	0.0699	0.0729	0.0692	0.0699	0.0729
Sens 4	43%	67%	25%	41%	100%	35%	40%	50%	42%
Spec 4	71%	71%	70%	71%	71%	70%	71%	71%	70%
Cutoff 5	0.0839	0.0839	0.0839	0.0839	0.0839	0.0839	0.0839	0.0839	0.0839
Sens 5	43%	67%	25%	29%	50%	29%	33%	25%	33%
Spec 5	80%	80%	81%	80%	80%	81%	80%	80%	81%
Cutoff 6	0.129	0.133	0.134	0.129	0.133	0.134	0.129	0.133	0.134
Sens 6	29%	33%	25%	18%	50%	12%	20%	25%	17%
Spec 6	90%	90%	91%	90%	90%	91%	90%	90%	91%
OR Quart 2	0.98	0	>1.0	2.1	>0	1.4	1.2	0.98	1.3
p Value	0.99	na	<1.0	0.41	<na	0.69	0.75	0.99	0.72
95% CI of	0.059	na	>0.060	0.36	>na	0.29	0.32	0.060	0.28
OR Quart 2	16	na	na	12	na	6.5	5.0	16	6.4
OR Quart 3	2.0	0	>2.1	2.7	>1.0	1.8	0.23	1.0	0.31
p Value	0.56	na	<0.56	0.26	<0.99	0.46	0.20	1.0	0.32
95% CI of	0.18	na	>0.18	0.49	>0.062	0.39	0.025	0.061	0.031
OR Quart 3	23	na	na	14	na	7.8	2.2	16	3.1
OR Quart 4	3.1	2.0	>1.0	3.3	>1.0	1.8	1.2	0.98	1.3
p Value	0.34	0.58	<1.0	0.16	<0.99	0.46	0.75	0.99	0.72
95% CI of	0.31	0.18	>0.060	0.63	>0.062	0.39	0.32	0.060	0.28
OR Quart 4	31	23	na	17	na	7.8	5.0	16	6.4

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	184000	178000	184000	185000	184000	156000
Average	189000	187000	189000	191000	189000	158000
Stdev	70300	63200	70300	93000	70300	51300
p (t-test)		0.90		0.91		0.060
Min	791	93200	791	190	791	49200
Max	520000	316000	520000	506000	520000	280000
n (Samp)	285	16	285	28	285	19
n (Patient)	163	16	163	28	163	19
sCr only						
Median	181000	243000	181000	232000	181000	175000
Average	184000	236000	184000	295000	184000	190000
Stdev	68800	73300	68800	135000	68800	53400
p (t-test)		0.14		5.0E-4		0.86
Min	190	140000	190	160000	190	140000
Max	520000	316000	520000	506000	520000	280000
n (Samp)	356	4	356	5	356	5
n (Patient)	197	4	197	5	197	5
UO only						
Median	183000	172000	183000	177000	183000	156000
Average	188000	168000	188000	169000	188000	155000
Stdev	72400	51800	72400	65000	72400	47600
p (t-test)		0.32		0.19		0.058
Min	791	93200	791	190	791	49200
Max	520000	282000	520000	331000	520000	230000
n (Samp)	261	13	261	26	261	17
n (Patient)	143	13	143	26	143	17

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.49	0.73	0.41	0.48	0.79	0.43	0.36	0.51	0.36
SE	0.075	0.15	0.085	0.058	0.12	0.061	0.070	0.13	0.074
p	0.92	0.12	0.29	0.79	0.015	0.25	0.041	0.91	0.052
nCohort 1	285	356	261	285	356	261	285	356	261
nCohort 2	16	4	13	28	5	26	19	5	17
Cutoff 1	152000	230000	133000	158000	230000	130000	139000	166000	144000
Sens 1	75%	75%	77%	71%	80%	73%	74%	80%	71%

TABLE 6-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Spec 1	30%	81%	21%	32%	81%	19%	21%	41%	26%
Cutoff 2	133000	140000	121000	125000	230000	121000	107000	166000	107000
Sens 2	81%	100%	85%	82%	80%	81%	84%	80%	82%
Spec 2	19%	24%	14%	14%	81%	14%	8%	41%	9%
Cutoff 3	95600	140000	95600	91800	160000	91800	91800	140000	91800
Sens 3	94%	100%	92%	93%	100%	92%	95%	100%	94%
Spec 3	6%	24%	6%	5%	37%	5%	5%	24%	5%
Cutoff 4	214000	207000	214000	214000	207000	214000	214000	207000	214000
Sens 4	25%	75%	8%	29%	80%	19%	11%	20%	12%
Spec 4	70%	71%	70%	70%	71%	70%	70%	71%	70%
Cutoff 5	233000	228000	233000	233000	228000	233000	233000	228000	233000
Sens 5	19%	75%	8%	14%	80%	12%	5%	20%	0%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	266000	262000	265000	266000	262000	265000	266000	262000	265000
Sens 6	12%	25%	8%	11%	40%	4%	5%	20%	0%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.75	0	3.1	1.0	>1.0	2.1	2.1	2.0	1.5
p Value	0.71	na	0.33	0.98	<0.99	0.24	0.41	0.57	0.64
95% CI of	0.16	na	0.32	0.34	>0.062	0.61	0.37	0.18	0.25
OR Quart 2	3.5	na	31	3.0	na	7.4	12	23	9.5
OR Quart 3	1.3	0	5.3	0.86	>0	1.3	3.8	1.0	3.8
p Value	0.72	na	0.13	0.79	<na	0.73	0.11	1.0	0.11
95% CI of	0.33	na	0.60	0.27	>na	0.33	0.75	0.062	0.76
OR Quart 3	5.0	na	47	2.7	na	4.9	19	16	19
OR Quart 4	1.0	3.1	4.2	1.2	>4.1	2.5	3.2	0.99	2.7
p Value	0.98	0.34	0.20	0.77	<0.21	0.15	0.17	0.99	0.25
95% CI of	0.24	0.31	0.46	0.40	>0.45	0.72	0.62	0.061	0.50
OR Quart 4	4.2	30	39	3.4	na	8.4	16	16	14

Myeloid differentiation primary response protein MyD88

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.000368	0.000245	0.000368	0.000368	0.000368	0.000368
Average	0.00279	0.000236	0.00279	0.000326	0.00279	0.000351
Stdev	0.0186	1.14E−5	0.0186	9.54E−5	0.0186	0.000109
p (t-test)		0.68		0.59		0.70
Min	0.000126	0.000224	0.000126	0.000224	0.000126	0.000224
Max	0.194	0.000245	0.194	0.000457	0.194	0.000457
n (Samp)	203	9	203	17	203	9
n (Patient)	120	9	120	17	120	9
sCr only						
Median	nd	nd	nd	nd	0.000368	0.000340
Average	nd	nd	nd	nd	0.00235	0.000340
Stdev	nd	nd	nd	nd	0.0169	0.000165
p (t-test)	nd	nd	nd	nd		0.87
Min	nd	nd	nd	nd	0.000126	0.000224
Max	nd	nd	nd	nd	0.194	0.000457
n (Samp)	nd	nd	nd	nd	246	2
n (Patient)	nd	nd	nd	nd	142	2
UO only						
Median	0.000368	0.000245	0.000368	0.000368	0.000368	0.000307
Average	0.00296	0.000236	0.00296	0.000326	0.00296	0.000337
Stdev	0.0193	1.14E−5	0.0193	9.54E−5	0.0193	0.000108
p (t-test)		0.67		0.57		0.70
Min	0.000126	0.000224	0.000126	0.000224	0.000126	0.000224
Max	0.194	0.000245	0.194	0.000457	0.194	0.000457
n (Samp)	189	9	189	17	189	8
n (Patient)	106	9	106	17	106	8

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.24	nd	0.25	0.47	nd	0.48	0.56	0.48	0.54
SE	0.095	nd	0.096	0.074	nd	0.074	0.10	0.21	0.11
p	0.0060	nd	0.0098	0.73	nd	0.82	0.54	0.94	0.74
nCohort 1	203	nd	189	203	nd	189	203	246	189
nCohort 2	9	nd	9	17	nd	17	9	2	8

TABLE 6-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Cutoff 1	0.000126	nd	0.000126	0.000224	nd	0.000224	0.000224	0.000126	0.000224
Sens 1	100%	nd	100%	76%	nd	76%	89%	100%	88%
Spec 1	0%	nd	1%	23%	nd	24%	23%	0%	24%
Cutoff 2	0.000126	nd	0.000126	0.000126	nd	0.000126	0.000224	0.000126	0.000224
Sens 2	100%	nd	100%	100%	nd	100%	89%	100%	88%
Spec 2	0%	nd	1%	0%	nd	1%	23%	0%	24%
Cutoff 3	0.000126	nd	0.000126	0.000126	nd	0.000126	0.000126	0.000126	0.000126
Sens 3	100%	nd	100%	100%	nd	100%	100%	100%	100%
Spec 3	0%	nd	1%	0%	nd	1%	0%	0%	1%
Cutoff 4	0.000368	nd	0.000368	0.000368	nd	0.000368	0.000368	0.000368	0.000368
Sens 4	0%	nd	0%	24%	nd	24%	44%	50%	38%
Spec 4	71%	nd	71%	71%	nd	71%	71%	73%	71%
Cutoff 5	0.000457	nd	0.000457	0.000457	nd	0.000457	0.000457	0.000457	0.000457
Sens 5	0%	nd	0%	0%	nd	0%	0%	0%	0%
Spec 5	96%	nd	95%	96%	nd	95%	96%	96%	95%
Cutoff 6	0.000457	nd	0.000457	0.000457	nd	0.000457	0.000457	0.000457	0.000457
Sens 6	0%	nd	0%	0%	nd	0%	0%	0%	0%
Spec 6	96%	nd	95%	96%	nd	95%	96%	96%	95%
OR Quart 2	>0	nd	>0	0.32	nd	1.3	4.2	0	3.1
p Value	<na	nd	<na	0.33	nd	0.70	0.20	na	0.33
95% CI of	>na	nd	>na	0.032	nd	0.33	0.46	na	0.31
OR Quart 2	na	nd	na	3.2	nd	5.2	39	na	31
OR Quart 3	>5.5	nd	>5.6	3.4	nd	1.0	0	0	1.0
p Value	<0.12	nd	<0.12	0.080	nd	1.0	na	na	1.0
95% CI of	>0.62	nd	>0.63	0.87	nd	0.24	na	na	0.061
OR Quart 3	na	nd	na	13	nd	4.2	na	na	16
OR Quart 4	>4.3	nd	>4.4	1.4	nd	1.0	4.2	1.0	3.1
p Value	<0.20	nd	<0.19	0.70	nd	0.98	0.20	1.0	0.34
95% CI of	>0.47	nd	>0.48	0.29	nd	0.24	0.46	0.061	0.31
OR Quart 4	na	nd	na	6.4	nd	4.3	39	16	31

TABLE 7

Comparison of marker levels in EDTA samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F).

Insulin-like growth factor 1 receptor

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0447	0.0717	nd	nd	0.0478	0.0804
Average	0.574	0.103	nd	nd	0.707	0.0835
Stdev	3.27	0.114	nd	nd	3.71	0.0515
p (t-test)		0.62	nd	nd		0.62
Min	0.000208	0.0214	nd	nd	0.000208	0.0214
Max	20.5	0.432	nd	nd	21.0	0.192
n (Samp)	39	12	nd	nd	32	9
n (Patient)	39	12	nd	nd	32	9

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.66	nd	0.71
SE	0.095	nd	0.11
p	0.088	nd	0.047
nCohort 1	39	nd	32
nCohort 2	12	nd	9
Cutoff 1	0.0331	nd	0.0545
Sens 1	75%	nd	78%
Spec 1	31%	nd	59%
Cutoff 2	0.0292	nd	0.0214
Sens 2	83%	nd	89%
Spec 2	28%	nd	25%
Cutoff 3	0.0214	nd	0.0179
Sens 3	92%	nd	100%
Spec 3	26%	nd	19%
Cutoff 4	0.0608	nd	0.0608
Sens 4	58%	nd	67%

TABLE 7-continued

Comparison of marker levels in EDTA samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F).

Spec 4	72%	nd	72%
Cutoff 5	0.0692	nd	0.0668
Sens 5	50%	nd	67%
Spec 5	82%	nd	81%
Cutoff 6	0.0945	nd	0.0839
Sens 6	33%	nd	44%
Spec 6	92%	nd	91%
OR Quart 2	0.91	nd	0
p Value	0.93	nd	na
95% CI of	0.11	nd	na
OR Quart 2	7.7	nd	na
OR Quart 3	0.91	nd	1.0
p Value	0.93	nd	1.0
95% CI of	0.11	nd	0.11
OR Quart 3	7.7	nd	8.9
OR Quart 4	4.3	nd	3.3
p Value	0.13	nd	0.23
95% CI of	0.66	nd	0.47
OR Quart 4	28	nd	23

Tumor necrosis factor ligand superfamily member 10

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0315	0.0228	nd	nd	0.0315	0.0228
Average	6.86	1.36	nd	nd	2.72	1.74
Stdev	27.8	5.65	nd	nd	5.07	6.41
p (t-test)		0.41	nd	nd		0.58
Min	0.0162	0.0162	nd	nd	0.0162	0.0162
Max	172	24.0	nd	nd	16.7	24.0
n (Samp)	38	18	nd	nd	32	14
n (Patient)	38	18	nd	nd	32	14

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.28	nd	0.29
SE	0.078	nd	0.088
p	0.0054	nd	0.017
nCohort 1	38	nd	32
nCohort 2	18	nd	14
Cutoff 1	0.0197	nd	0.0197
Sens 1	72%	nd	71%
Spec 1	18%	nd	16%
Cutoff 2	0	nd	0
Sens 2	100%	nd	100%
Spec 2	0%	nd	0%
Cutoff 3	0	nd	0
Sens 3	100%	nd	100%
Spec 3	0%	nd	0%
Cutoff 4	0.601	nd	0.444
Sens 4	6%	nd	7%
Spec 4	71%	nd	72%
Cutoff 5	6.98	nd	6.98
Sens 5	6%	nd	7%
Spec 5	82%	nd	81%
Cutoff 6	13.4	nd	10.8
Sens 6	6%	nd	7%
Spec 6	92%	nd	91%
OR Quart 2	2.2	nd	0.50
p Value	0.55	nd	0.59
95% CI of	0.17	nd	0.039
OR Quart 2	27	nd	6.4
OR Quart 3	17	nd	5.0
p Value	0.015	nd	0.096
95% CI of	1.8	nd	0.75
OR Quart 3	170	nd	33
OR Quart 4	13	nd	4.2
p Value	0.028	nd	0.15
95% CI of	1.3	nd	0.61
OR Quart 4	130	nd	29

TABLE 8

Comparison of the maximum marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in EDTA samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Heat shock 70 kDa protein 1

	0 hr prior to AKI stage		24 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO				
Median	618	2280	618	2280
Average	1400	2650	1400	2650
Stdev	2030	2030	2030	2030
p (t-test)		0.30		0.30
Min	0.288	840	0.288	840
Max	10000	4840	10000	4840
n (Samp)	53	3	53	3
n (Patient)	53	3	53	3
UO only				
Median	641	1560	641	1560
Average	1410	1560	1410	1560
Stdev	1930	1020	1930	1020
p (t-test)		0.92		0.92
Min	0.288	840	0.288	840
Max	10000	2280	10000	2280
n (Samp)	44	2	44	2
n (Patient)	44	2	44	2

	0 hr prior to AKI stage			24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.77	nd	0.66	0.77	nd	0.66
SE	0.16	nd	0.22	0.16	nd	0.22
p	0.093	nd	0.46	0.093	nd	0.46
nCohort 1	53	nd	44	53	nd	44
nCohort 2	3	nd	2	3	nd	2
Cutoff 1	837	nd	837	837	nd	837
Sens 1	100%	nd	100%	100%	nd	100%
Spec 1	57%	nd	55%	57%	nd	55%
Cutoff 2	837	nd	837	837	nd	837
Sens 2	100%	nd	100%	100%	nd	100%
Spec 2	57%	nd	55%	57%	nd	55%
Cutoff 3	837	nd	837	837	nd	837
Sens 3	100%	nd	100%	100%	nd	100%
Spec 3	57%	nd	55%	57%	nd	55%
Cutoff 4	1370	nd	1370	1370	nd	1370
Sens 4	67%	nd	50%	67%	nd	50%
Spec 4	72%	nd	70%	72%	nd	70%
Cutoff 5	2700	nd	2860	2700	nd	2860
Sens 5	33%	nd	0%	33%	nd	0%
Spec 5	81%	nd	82%	81%	nd	82%
Cutoff 6	3540	nd	3630	3540	nd	3630
Sens 6	33%	nd	0%	33%	nd	0%
Spec 6	91%	nd	91%	91%	nd	91%
OR Quart 2	>0	nd	>0	>0	nd	>0
p Value	<na	nd	<na	<na	nd	<na
95% CI of	>na	nd	>na	>na	nd	>na
OR Quart 2	na	nd	na	na	nd	na
OR Quart 3	>1.1	nd	>1.1	>1.1	nd	>1.1
p Value	<0.96	nd	<0.95	<0.96	nd	<0.95
95% CI of	>0.061	nd	>0.060	>0.061	nd	>0.060
OR Quart 3	na	nd	na	na	nd	na
OR Quart 4	>2.3	nd	>1.0	>2.3	nd	>1.0
p Value	<0.51	nd	<1.0	<0.51	nd	<1.0
95% CI of	>0.19	nd	>0.055	>0.19	nd	>0.055
OR Quart 4	na	nd	na	na	nd	na

TABLE 8-continued

Comparison of the maximum marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in EDTA samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	184000	172000	184000	172000	184000	167000
Average	188000	180000	188000	177000	188000	165000
Stdev	79000	49600	79000	44400	79000	20800
p (t-test)		0.78		0.69		0.57
Min	1370	111000	1370	111000	1370	140000
Max	520000	256000	520000	245000	520000	187000
n (Samp)	88	8	88	8	88	4
n (Patient)	88	8	88	8	88	4
sCr only						
Median	181000	177000	181000	177000	181000	167000
Average	187000	188000	187000	181000	187000	165000
Stdev	75100	49800	75100	38000	75100	23700
p (t-test)		0.98		0.88		0.61
Min	190	140000	190	140000	190	140000
Max	520000	256000	520000	230000	520000	187000
n (Samp)	164	4	164	4	164	3
n (Patient)	164	4	164	4	164	3
UO only						
Median	180000	162000	180000	162000	180000	158000
Average	187000	166000	187000	166000	187000	158000
Stdev	85300	45100	85300	45100	85300	18300
p (t-test)		0.56		0.56		0.56
Min	1080	111000	1080	111000	1080	140000
Max	520000	245000	520000	245000	520000	176000
n (Samp)	81	6	81	6	81	3
n (Patient)	81	6	81	6	81	3

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.47	0.50	0.41	0.47	0.48	0.41	0.39	0.38	0.36
SE	0.11	0.15	0.13	0.11	0.15	0.13	0.15	0.17	0.18
p	0.80	0.99	0.47	0.75	0.92	0.47	0.48	0.49	0.43
nCohort 1	88	164	81	88	164	81	88	164	81
nCohort 2	8	4	6	8	4	6	4	3	3
Cutoff 1	158000	165000	139000	158000	165000	139000	158000	139000	139000
Sens 1	75%	75%	83%	75%	75%	83%	75%	100%	100%
Spec 1	36%	40%	25%	36%	40%	25%	36%	22%	25%
Cutoff 2	139000	139000	139000	139000	139000	139000	139000	139000	139000
Sens 2	88%	100%	83%	88%	100%	83%	100%	100%	100%
Spec 2	24%	22%	25%	24%	22%	25%	24%	22%	25%
Cutoff 3	107000	139000	107000	107000	139000	107000	139000	139000	139000
Sens 3	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 3	11%	22%	12%	11%	22%	12%	24%	22%	25%
Cutoff 4	216000	217000	214000	216000	217000	214000	216000	217000	214000
Sens 4	25%	25%	17%	25%	25%	17%	0%	0%	0%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	227000	230000	227000	227000	230000	227000	227000	230000	227000
Sens 5	25%	25%	17%	25%	0%	17%	0%	0%	0%
Spec 5	81%	80%	80%	81%	80%	80%	81%	80%	80%
Cutoff 6	272000	272000	258000	272000	272000	258000	272000	272000	258000
Sens 6	0%	0%	0%	0%	0%	0%	0%	0%	0%
Spec 6	91%	90%	90%	91%	90%	90%	91%	90%	90%
OR Quart 2	0.48	1.0	0	0.48	1.0	0	>1.0	>1.0	>0
p Value	0.56	1.0	na	0.56	1.0	na	<0.98	<0.99	<na
95% CI of	0.040	0.060	na	0.040	0.060	na	>0.062	>0.062	>na
OR Quart 2	5.7	17	na	5.7	17	na	na	na	na
OR Quart 3	1.6	1.0	4.7	1.6	1.0	4.7	>2.2	>1.0	>2.2
p Value	0.64	1.0	0.19	0.64	1.0	0.19	<0.53	<0.99	<0.53
95% CI of	0.24	0.060	0.48	0.24	0.060	0.48	>0.18	>0.062	>0.19
OR Quart 3	10	17	46	10	17	46	na	na	na
OR Quart 4	1.0	1.0	1.0	1.0	1.0	1.0	>1.0	>1.0	>1.0

TABLE 8-continued

Comparison of the maximum marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in EDTA samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

p Value	1.0	1.0	0.97	1.0	1.0	0.97	<0.98	<0.97	<0.97
95% CI of	0.13	0.060	0.061	0.13	0.060	0.061	>0.062	>0.064	>0.061
OR Quart 4	7.7	17	18	7.7	17	18	na	na	na

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0228	0.0271	0.0228	0.0271	0.0228	0.0228
Average	11.3	3.14	11.3	3.14	11.3	2.39
Stdev	50.4	7.16	50.4	7.16	50.4	5.88
p (t-test)		0.58		0.58		0.64
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	20.9	292	20.9	292	15.7
n (Samp)	69	12	69	12	69	7
n (Patient)	69	12	69	12	69	7
sCr only						
Median	0.0313	0.0228	0.0313	0.0228	0.0313	0.0228
Average	9.00	2.64	9.00	2.64	9.00	5.25
Stdev	37.6	6.40	37.6	6.40	37.6	9.06
p (t-test)		0.68		0.68		0.86
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	15.7	292	15.7	292	15.7
n (Samp)	138	6	138	6	138	3
n (Patient)	138	6	138	6	138	3
UO only						
Median	0.0313	0.0271	0.0313	0.0271	0.0313	0.0228
Average	13.0	2.74	13.0	2.74	13.0	0.173
Stdev	51.4	7.33	51.4	7.33	51.4	0.367
p (t-test)		0.58		0.58		0.55
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	292	20.9	292	20.9	292	0.921
n (Samp)	67	8	67	8	67	6
n (Patient)	67	8	67	8	67	6

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.50	0.37	0.44	0.50	0.37	0.44	0.48	0.41	0.35
SE	0.091	0.12	0.11	0.091	0.12	0.11	0.12	0.18	0.13
p	0.96	0.30	0.59	0.96	0.30	0.59	0.85	0.60	0.25
nCohort 1	69	138	67	69	138	67	69	138	67
nCohort 2	12	6	8	12	6	8	7	3	6
Cutoff 1	0.0197	0.0205	0.0197	0.0197	0.0205	0.0197	0.0197	0	0.0197
Sens 1	92%	83%	88%	92%	83%	88%	86%	100%	83%
Spec 1	17%	14%	12%	17%	14%	12%	17%	0%	12%
Cutoff 2	0.0197	0.0205	0.0197	0.0197	0.0205	0.0197	0.0197	0	0.0197
Sens 2	92%	83%	88%	92%	83%	88%	86%	100%	83%
Spec 2	17%	14%	12%	17%	14%	12%	17%	0%	12%
Cutoff 3	0.0197	0	0	0.0197	0	0	0	0	0
Sens 3	92%	100%	100%	92%	100%	100%	100%	100%	100%
Spec 3	17%	0%	0%	17%	0%	0%	0%	0%	0%
Cutoff 4	0.0392	0.921	0.0591	0.0392	0.921	0.0591	0.0392	0.921	0.0591
Sens 4	25%	17%	25%	25%	17%	25%	29%	33%	17%
Spec 4	71%	70%	70%	71%	70%	70%	71%	70%	70%
Cutoff 5	2.12	3.82	3.20	2.12	3.82	3.20	2.12	3.82	3.20
Sens 5	17%	17%	12%	17%	17%	12%	14%	33%	0%
Spec 5	81%	80%	81%	81%	80%	81%	81%	80%	81%
Cutoff 6	5.31	15.7	23.0	5.31	15.7	23.0	5.31	15.7	23.0
Sens 6	17%	0%	0%	17%	0%	0%	14%	0%	0%
Spec 6	91%	91%	91%	91%	91%	91%	91%	91%	91%
OR Quart 2	6.3	0	2.1	6.3	0	2.1	0.47	0	>2.4
p Value	0.11	na	0.55	0.11	na	0.55	0.55	na	<0.50
95% CI of	0.67	na	0.18	0.67	na	0.18	0.039	na	>0.20
OR Quart 2	60	na	26	60	na	26	5.7	na	na
OR Quart 3	3.4	4.4	1.0	3.4	4.4	1.0	1.6	1.0	>0
p Value	0.31	0.20	1.0	0.31	0.20	1.0	0.63	0.98	<na
95% CI of	0.32	0.46	0.058	0.32	0.46	0.058	0.23	0.062	>na

TABLE 8-continued

Comparison of the maximum marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in EDTA samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

OR Quart 3	35	41	17	35	41	17	11	17	na
OR Quart 4	3.2	1.0	5.1	3.2	1.0	5.1	0.47	1.0	>5.4
p Value	0.34	1.0	0.16	0.34	1.0	0.16	0.55	0.98	<0.15
95% CI of	0.30	0.060	0.52	0.30	0.060	0.52	0.039	0.062	>0.55
OR Quart 4	33	17	51	33	17	51	5.7	17	na

TABLE 9

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Stromelysin-1:Metalloproteinase inhibitor 2 complex

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	0.487	0.487
Average	177	40.1
Stdev	1320	100
p (t-test)		0.79
Min	0.237	0.487
Max	13900	267
n (Samp)	113	7
n (Patient)	87	7
sCr only		
Median	0.487	10.9
Average	171	181
Stdev	1290	303
p (t-test)		0.99
Min	0.237	0.487
Max	13900	530
n (Samp)	118	3
n (Patient)	91	3
UO only		
Median	0.237	0.487
Average	190	53.8
Stdev	1430	119
p (t-test)		0.83
Min	0.237	0.487
Max	13900	267
n (Samp)	96	5
n (Patient)	74	5

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.71	0.81	0.73
SE	0.11	0.15	0.13
p	0.063	0.046	0.081
nCohort 1	113	118	96
nCohort 2	7	3	5
Cutoff 1	0.237	0.237	0.237
Sens 1	100%	100%	100%
Spec 1	45%	43%	52%
Cutoff 2	0.237	0.237	0.237
Sens 2	100%	100%	100%
Spec 2	45%	43%	52%
Cutoff 3	0.237	0.237	0.237
Sens 3	100%	100%	100%
Spec 3	45%	43%	52%
Cutoff 4	0.487	0.487	0.487
Sens 4	29%	67%	20%
Spec 4	82%	82%	82%
Cutoff 5	0.487	0.487	0.487

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Sens 5	29%	67%	20%
Spec 5	82%	82%	82%
Cutoff 6	123	154	118
Sens 6	14%	33%	20%
Spec 6	90%	91%	91%
OR Quart 2	>6.0	>1.0	>0
p Value	<0.11	<0.98	<na
95% CI of	>0.66	>0.062	>na
OR Quart 2	na	na	na
OR Quart 3	>0	>0	>4.8
p Value	<na	<na	<0.18
95% CI of	>na	>na	>0.49
OR Quart 3	na	na	na
OR Quart 4	>2.1	>2.1	>1.0
p Value	<0.54	<0.56	<1.0
95% CI of	>0.18	>0.18	>0.059
OR Quart 4	na	na	na

Heat shock 70 kDa protein 1

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	277	1420
Average	581	2850
Stdev	1100	4410
p (t-test)		2.0E−4
Min	0.297	250
Max	7800	11800
n (Samp)	111	6
n (Patient)	86	6
sCr only		
Median	289	1510
Average	686	1440
Stdev	1500	318
p (t-test)		0.39
Min	0.297	1090
Max	11800	1710
n (Samp)	115	3
n (Patient)	89	3
UO only		
Median	267	934
Average	617	3480
Stdev	1170	5560
p (t-test)		3.5E−4
Min	0.297	250
Max	7800	11800
n (Samp)	96	4
n (Patient)	74	4

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.83	0.92	0.77
SE	0.10	0.11	0.14
p	0.0018	1.9E−4	0.055
nCohort 1	111	115	96
nCohort 2	6	3	4
Cutoff 1	529	1040	529
Sens 1	83%	100%	75%
Spec 1	70%	89%	70%
Cutoff 2	529	1040	246
Sens 2	83%	100%	100%
Spec 2	70%	89%	49%
Cutoff 3	246	1040	246
Sens 3	100%	100%	100%
Spec 3	48%	89%	49%
Cutoff 4	529	596	574
Sens 4	83%	100%	50%

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Spec 4	70%	70%	71%
Cutoff 5	770	782	782
Sens 5	67%	100%	50%
Spec 5	80%	80%	80%
Cutoff 6	1040	1320	1340
Sens 6	67%	67%	25%
Spec 6	90%	91%	91%
OR Quart 2	>1.0	>0	>1.0
p Value	<0.98	<na	<0.98
95% CI of	>0.062	>na	>0.062
OR Quart 2	na	na	na
OR Quart 3	>1.0	>0	>1.0
p Value	<0.98	<na	<0.98
95% CI of	>0.062	>na	>0.062
OR Quart 3	na	na	na
OR Quart 4	>4.5	>3.2	>2.2
p Value	<0.19	<0.32	<0.54
95% CI of	>0.47	>0.32	>0.18
OR Quart 4	na	na	na

Insulin-like growth factor 1 receptor

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	0.0103	0.0103
Average	0.0227	0.0647
Stdev	0.0655	0.132
p (t-test)		0.13
Min	0.000123	0.00862
Max	0.679	0.365
n (Samp)	112	7
n (Patient)	88	7
sCr only		
Median	0.0103	0.0197
Average	0.0261	0.0160
Stdev	0.0718	0.00637
p (t-test)		0.81
Min	0.000123	0.00862
Max	0.679	0.0197
n (Samp)	117	3
n (Patient)	92	3
UO only		
Median	0.0103	0.0103
Average	0.0239	0.0849
Stdev	0.0705	0.157
p (t-test)		0.083
Min	0.000123	0.0103
Max	0.679	0.365
n (Samp)	96	5
n (Patient)	76	5

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.61	0.57	0.65
SE	0.12	0.17	0.14
p	0.34	0.71	0.28
nCohort 1	112	117	96
nCohort 2	7	3	5
Cutoff 1	0.00862	0.00573	0.00862
Sens 1	86%	100%	100%
Spec 1	41%	32%	44%
Cutoff 2	0.00862	0.00573	0.00862
Sens 2	86%	100%	100%
Spec 2	41%	32%	44%
Cutoff 3	0.00573	0.00573	0.00862
Sens 3	100%	100%	100%
Spec 3	33%	32%	44%

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Cutoff 4	0.0197	0.0211	0.0211
Sens 4	29%	0%	40%
Spec 4	71%	71%	72%
Cutoff 5	0.0292	0.0292	0.0292
Sens 5	14%	0%	20%
Spec 5	82%	81%	82%
Cutoff 6	0.0423	0.0423	0.0423
Sens 6	14%	0%	20%
Spec 6	92%	91%	92%
OR Quart 2	>4.5	>1.0	>1.0
p Value	<0.19	<0.98	<0.98
95% CI of	>0.47	>0.062	>0.062
OR Quart 2	na	na	na
OR Quart 3	>1.0	>2.1	>2.2
p Value	<1.0	<0.54	<0.54
95% CI of	>0.060	>0.18	>0.18
OR Quart 3	na	na	na
OR Quart 4	>2.1	>0	>2.1
p Value	<0.56	<na	<0.56
95% CI of	>0.18	>na	>0.18
OR Quart 4	na	na	na

Interstitial collagenase:Metalloproteinase inhibitor2 complex

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	0.233	6.17
Average	152	50.7
Stdev	1510	110
p (t-test)		0.86
Min	0.228	0.228
Max	16000	297
n (Samp)	113	7
n (Patient)	87	7
sCr only		
Median	0.233	6.97
Average	149	12.2
Stdev	1470	15.3
p (t-test)		0.87
Min	0.228	0.233
Max	16000	29.5
n (Samp)	118	3
n (Patient)	91	3
UO only		
Median	0.233	6.17
Average	173	69.6
Stdev	1630	129
p (t-test)		0.89
Min	0.228	0.228
Max	16000	297
n (Samp)	96	5
n (Patient)	74	5

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.66	0.79	0.62
SE	0.12	0.16	0.14
p	0.17	0.072	0.37
nCohort 1	113	118	96
nCohort 2	7	3	5
Cutoff 1	0.228	0.228	0
Sens 1	71%	100%	100%
Spec 1	38%	39%	0%
Cutoff 2	0	0.228	0
Sens 2	100%	100%	100%
Spec 2	0%	39%	0%
Cutoff 3	0	0.228	0

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Sens 3	100%	100%	100%
Spec 3	0%	39%	0%
Cutoff 4	0.233	0.233	0.233
Sens 4	57%	67%	60%
Spec 4	80%	79%	79%
Cutoff 5	1.26	1.35	1.26
Sens 5	57%	67%	60%
Spec 5	81%	81%	80%
Cutoff 6	14.2	18.5	10.7
Sens 6	29%	33%	40%
Spec 6	90%	92%	91%
OR Quart 2	>2.1	>0	0
p Value	<0.54	<na	na
95% CI of	>0.18	>na	na
OR Quart 2	na	na	na
OR Quart 3	>1.0	>1.0	0
p Value	<0.98	<0.98	na
95% CI of	>0.062	>0.062	na
OR Quart 3	na	na	na
OR Quart 4	>4.6	>2.1	1.5
p Value	<0.18	<0.56	0.67
95% CI of	>0.48	>0.18	0.23
OR Quart 4	na	na	9.8

72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	29.2	295
Average	793	2740
Stdev	2550	5880
p (t-test)		0.081
Min	1.15	1.15
Max	16000	16000
n (Samp)	108	7
n (Patient)	86	7
sCr only		
Median	30.3	527
Average	926	447
Stdev	2880	245
p (t-test)		0.77
Min	1.15	171
Max	16000	642
n (Samp)	113	3
n (Patient)	90	3
UO only		
Median	28.1	295
Average	868	3670
Stdev	2710	6930
p (t-test)		0.044
Min	1.15	1.15
Max	16000	16000
n (Samp)	95	5
n (Patient)	76	5

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.70	0.74	0.67
SE	0.11	0.17	0.14
p	0.081	0.16	0.21
nCohort 1	108	113	95
nCohort 2	7	3	5
Cutoff 1	234	164	234
Sens 1	71%	100%	80%
Spec 1	71%	65%	69%
Cutoff 2	164	164	234
Sens 2	86%	100%	80%

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Spec 2	67%	65%	69%
Cutoff 3	0	164	0
Sens 3	100%	100%	100%
Spec 3	0%	65%	0%
Cutoff 4	227	365	365
Sens 4	71%	67%	40%
Spec 4	70%	71%	71%
Cutoff 5	595	656	595
Sens 5	43%	0%	40%
Spec 5	81%	81%	80%
Cutoff 6	1700	1780	1700
Sens 6	29%	0%	40%
Spec 6	91%	90%	91%
OR Quart 2	0	>0	0
p Value	na	<na	na
95% CI of	na	>na	na
OR Quart 2	na	na	na
OR Quart 3	3.1	>1.0	2.1
p Value	0.34	<0.98	0.56
95% CI of	0.30	>0.062	0.18
OR Quart 3	32	na	25
OR Quart 4	3.1	>2.1	2.1
p Value	0.34	<0.54	0.56
95% CI of	0.30	>0.18	0.18
OR Quart 4	32	na	25

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	2720	3990	2720	2690	2720	2100
Average	3340	4390	3340	6270	3340	2870
Stdev	2880	3520	2880	11900	2880	2900
p (t-test)		0.093		5.4E−5		0.60
Min	0.234	171	0.234	375	0.234	138
Max	48400	15000	48400	55700	48400	9700
n (Samp)	1261	22	1261	20	1261	10
n (Patient)	450	22	450	20	450	10
sCr only						
Median	2780	2260	2780	3970	2780	3900
Average	3450	2670	3450	3650	3450	3740
Stdev	3260	2170	3260	2070	3260	2410
p (t-test)		0.50		0.90		0.86
Min	0.234	171	0.234	1090	0.234	963
Max	55700	6800	55700	5590	55700	6210
n (Samp)	1325	8	1325	4	1325	4
n (Patient)	465	8	465	4	465	4
UO only						
Median	2840	4560	2840	4560	2840	3280
Average	3410	6830	3410	8190	3410	3570
Stdev	2840	6750	2840	12900	2840	3190
p (t-test)		1.4E−5		3.0E−10		0.88
Min	0.234	416	0.234	375	0.234	346
Max	48400	26600	48400	55700	48400	9700
n (Samp)	1116	14	1116	19	1116	7
n (Patient)	364	14	364	19	364	7

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.59	0.42	0.70	0.55	0.58	0.62	0.40	0.57	0.48
SE	0.064	0.11	0.079	0.067	0.15	0.069	0.095	0.15	0.11
p	0.16	0.44	0.010	0.45	0.59	0.084	0.32	0.65	0.88
nCohort 1	1261	1325	1116	1261	1325	1116	1261	1325	1116
nCohort 2	22	8	14	20	4	19	10	4	7
Cutoff 1	2200	1340	3860	2030	2870	2080	1180	2560	1650
Sens 1	73%	75%	71%	70%	75%	74%	70%	75%	71%

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Spec 1	39%	19%	67%	35%	52%	34%	16%	46%	24%
Cutoff 2	1340	623	2310	1740	1090	1740	957	957	1180
Sens 2	82%	88%	86%	80%	100%	84%	80%	100%	86%
Spec 2	20%	5%	39%	28%	14%	26%	11%	10%	14%
Cutoff 3	623	169	1490	1110	1090	1110	341	957	325
Sens 3	91%	100%	93%	90%	100%	95%	90%	100%	100%
Spec 3	5%	0%	21%	15%	14%	13%	1%	10%	1%
Cutoff 4	3940	4040	4060	3940	4040	4060	3940	4040	4060
Sens 4	55%	12%	57%	45%	50%	58%	20%	50%	29%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	4850	4930	4910	4850	4930	4910	4850	4930	4910
Sens 5	41%	12%	43%	35%	50%	42%	20%	50%	29%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	6440	6520	6470	6440	6520	6470	6440	6520	6470
Sens 6	23%	12%	29%	20%	0%	32%	10%	0%	14%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.33	2.0	0.50	1.5	0	1.7	1.0	1.0	1.0
p Value	0.17	0.57	0.57	0.53	na	0.48	1.0	1.0	1.0
95% CI of	0.066	0.18	0.045	0.42	na	0.40	0.14	0.062	0.14
OR Quart 2	1.6	22	5.5	5.4	na	7.1	7.1	16	7.1
OR Quart 3	0.83	2.0	2.0	0.50	1.0	0.33	1.0	0	0
p Value	0.76	0.57	0.42	0.42	1.0	0.34	1.0	na	na
95% CI of	0.25	0.18	0.37	0.090	0.062	0.034	0.14	na	na
OR Quart 3	2.7	22	11	2.7	16	3.2	7.1	na	na
OR Quart 4	1.5	3.0	3.6	2.0	2.0	3.4	2.0	2.0	1.5
p Value	0.44	0.34	0.12	0.26	0.57	0.065	0.42	0.57	0.65
95% CI of	0.53	0.31	0.73	0.60	0.18	0.93	0.37	0.18	0.25
OR Quart 4	4.3	29	17	6.8	22	13	11	22	9.1

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0285	0.0287	0.0285	0.0387	0.0285	0.0287
Average	2.55	7.89	2.55	9.52	2.55	0.125
Stdev	9.75	24.9	9.75	30.0	9.75	0.289
p (t-test)		0.017		0.0029		0.46
Min	0.0110	0.0139	0.0110	0.0110	0.0110	0.0205
Max	159	113	159	134	159	0.894
n (Samp)	1234	21	1234	20	1234	9
n (Patient)	456	21	456	20	456	9
sCr only						
Median	0.0285	0.0243	0.0285	1.57	0.0285	0.0287
Average	2.78	1.22	2.78	1.66	2.78	0.0300
Stdev	10.9	3.38	10.9	1.89	10.9	0.00805
p (t-test)		0.69		0.84		0.62
Min	0.0110	0.0139	0.0110	0.0227	0.0110	0.0217
Max	159	9.58	159	3.47	159	0.0410
n (Samp)	1294	8	1294	4	1294	4
n (Patient)	471	8	471	4	471	4
UO only						
Median	0.0285	0.0311	0.0285	0.0410	0.0285	0.0363
Average	2.57	13.5	2.57	15.4	2.57	0.153
Stdev	9.97	27.1	9.97	38.8	9.97	0.327
p (t-test)		8.5E−5		6.1E−7		0.52
Min	0.0110	0.0139	0.0110	0.0110	0.0110	0.0205
Max	159	79.6	159	134	159	0.894
n (Samp)	1092	14	1092	19	1092	7
n (Patient)	372	14	372	19	372	7

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.57	0.45	0.59	0.61	0.58	0.61	0.46	0.49	0.48
SE	0.066	0.11	0.081	0.068	0.15	0.069	0.099	0.15	0.11
p	0.30	0.61	0.25	0.12	0.59	0.098	0.72	0.95	0.85
nCohort 1	1234	1294	1092	1234	1294	1092	1234	1294	1092

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

nCohort 2	21	8	14	20	4	19	9	4	7
Cutoff 1	0.0247	0.0239	0.0285	0.0247	0.0239	0.0247	0.0217	0.0285	0.0237
Sens 1	76%	88%	71%	70%	75%	74%	78%	75%	71%
Spec 1	41%	33%	51%	41%	33%	40%	22%	52%	28%
Cutoff 2	0.0239	0.0239	0.0247	0.0217	0.0217	0.0205	0.0205	0.0205	0.0217
Sens 2	81%	88%	86%	80%	100%	89%	89%	100%	86%
Spec 2	37%	33%	40%	22%	22%	17%	19%	18%	21%
Cutoff 3	0.0239	0.0110	0.0110	0.0205	0.0217	0.0162	0.0162	0.0205	0.0162
Sens 3	90%	100%	100%	90%	100%	95%	100%	100%	100%
Spec 3	34%	3%	3%	19%	22%	14%	15%	18%	14%
Cutoff 4	0.0439	0.0410	0.0439	0.0439	0.0410	0.0439	0.0439	0.0410	0.0439
Sens 4	24%	12%	29%	45%	50%	47%	11%	0%	14%
Spec 4	74%	70%	74%	74%	70%	74%	74%	70%	74%
Cutoff 5	0.0597	0.0597	0.0597	0.0597	0.0597	0.0597	0.0597	0.0597	0.0597
Sens 5	24%	12%	29%	45%	50%	47%	11%	0%	14%
Spec 5	80%	80%	81%	80%	80%	81%	80%	80%	81%
Cutoff 6	5.80	5.86	5.80	5.80	5.86	5.80	5.80	5.86	5.80
Sens 6	19%	12%	29%	15%	0%	16%	0%	0%	0%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	3.0	1.0	1.00	0.39	1.00	0.20	4.0	>3.0	3.0
p Value	0.18	1.00	1.00	0.27	1.00	0.14	0.21	<0.34	0.34
95% CI of	0.61	0.062	0.14	0.076	0.062	0.023	0.45	>0.31	0.31
OR Quart 2	15	16	7.1	2.1	16	1.7	36	na	29
OR Quart 3	4.1	5.1	3.0	0.80	0	0.79	2.0	>0	1.0
p Value	0.078	0.14	0.18	0.74	na	0.73	0.57	<na	1.0
95% CI of	0.86	0.59	0.61	0.21	na	0.21	0.18	>na	0.062
OR Quart 3	19	44	15	3.0	na	3.0	22	na	16
OR Quart 4	2.5	1.0	2.0	1.8	2.0	1.8	2.0	>1.0	2.0
p Value	0.27	1.00	0.42	0.29	0.57	0.29	0.57	<1.00	0.57
95% CI of	0.48	0.062	0.36	0.60	0.18	0.60	0.18	>0.063	0.18
OR Quart 4	13	16	11	5.5	22	5.5	22	na	22

Myeloid differentiation primary response protein MyD88

	0 hr prior to AKI stage		24 hr prior to AKI stage	
sCr or UO	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.000533	0.000146	0.000533	0.000165
Average	0.0162	0.000146	0.0162	0.00319
Stdev	0.0567	2.76E−5	0.0567	0.00825
p (t-test)		0.69		0.52
Min	0.000126	0.000126	0.000126	0.000165
Max	0.671	0.000165	0.671	0.0236
n (Samp)	247	2	247	8
n (Patient)	141	2	141	8

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr only		
Median	0.000533	0.000165
Average	0.0159	0.000288
Stdev	0.0562	0.000213
p (t-test)		0.63
Min	0.000126	0.000165
Max	0.671	0.000533
n (Samp)	252	3
n (Patient)	145	3
UO only		
Median	0.000533	0.000165
Average	0.0141	0.000239
Stdev	0.0390	0.000165
p (t-test)		0.43
Min	0.000126	0.000165
Max	0.371	0.000533
n (Samp)	233	5
n (Patient)	128	5

TABLE 9-continued

Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in urine samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

	0 hr prior to AKI stage			24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.13	nd	nd	0.38	0.33	0.28
SE	0.16	nd	nd	0.11	0.17	0.13
p	0.027	nd	nd	0.25	0.33	0.093
nCohort 1	247	nd	nd	247	252	233
nCohort 2	2	nd	nd	8	3	5
Cutoff 1	0	nd	nd	0.000126	0.000126	0.000126
Sens 1	100%	nd	nd	100%	100%	100%
Spec 1	0%	nd	nd	11%	10%	12%
Cutoff 2	0	nd	nd	0.000126	0.000126	0.000126
Sens 2	100%	nd	nd	100%	100%	100%
Spec 2	0%	nd	nd	11%	10%	12%
Cutoff 3	0	nd	nd	0.000126	0.000126	0.000126
Sens 3	100%	nd	nd	100%	100%	100%
Spec 3	0%	nd	nd	11%	10%	12%
Cutoff 4	0.00247	nd	nd	0.00247	0.00237	0.00616
Sens 4	0%	nd	nd	12%	0%	0%
Spec 4	70%	nd	nd	70%	70%	71%
Cutoff 5	0.0184	nd	nd	0.0184	0.0184	0.0190
Sens 5	0%	nd	nd	12%	0%	0%
Spec 5	80%	nd	nd	80%	81%	80%
Cutoff 6	0.0393	nd	nd	0.0393	0.0387	0.0387
Sens 6	0%	nd	nd	0%	0%	0%
Spec 6	90%	nd	nd	90%	90%	90%
OR Quart 2	>0	nd	nd	2.0	>0	>1.0
p Value	<na	nd	nd	0.57	<na	<0.98
95% CI of	>na	nd	nd	0.18	>na	>0.063
OR Quart 2	na	nd	nd	23	na	na
OR Quart 3	>0	nd	nd	5.3	>3.1	>0
p Value	<na	nd	nd	0.13	<0.33	<na
95% CI of	>na	nd	nd	0.61	>0.32	>na
OR Quart 3	na	nd	nd	47	na	na
OR Quart 4	>2.1	nd	nd	0	>0	>4.4
p Value	<0.55	nd	nd	na	<na	<0.19
95% CI of	>0.19	nd	nd	na	>na	>0.47
OR Quart 4	na	nd	nd	na	na	na

TABLE 10

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Heat shock 70 kDa protein 1

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	905	1560
Average	1560	1560
Stdev	2100	1020
p (t-test)		1.00
Min	0.288	840
Max	10700	2280
n (Samp)	129	2
n (Patient)	106	2
UO only		
Median	929	1560
Average	1550	1560
Stdev	2080	1020
p (t-test)		1.00
Min	0.288	840

TABLE 10-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Max	10700	2280
n (Samp)	113	2
n (Patient)	90	2

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.64	nd	0.64
SE	0.21	nd	0.21
p	0.51	nd	0.52
nCohort 1	129	nd	113
nCohort 2	2	nd	2
Cutoff 1	837	nd	837
Sens 1	100%	nd	100%
Spec 1	49%	nd	49%
Cutoff 2	837	nd	837
Sens 2	100%	nd	100%
Spec 2	49%	nd	49%
Cutoff 3	837	nd	837
Sens 3	100%	nd	100%
Spec 3	49%	nd	49%
Cutoff 4	1560	nd	1560
Sens 4	50%	nd	50%
Spec 4	71%	nd	71%
Cutoff 5	2550	nd	2550
Sens 5	0%	nd	0%
Spec 5	81%	nd	81%
Cutoff 6	3630	nd	3540
Sens 6	0%	nd	0%
Spec 6	91%	nd	90%
OR Quart 2	>1.0	nd	>1.0
p Value	<1.0	nd	<1.0
95% CI of	>0.060	nd	>0.060
OR Quart 2	na	nd	na
OR Quart 3	>0	nd	>0
p Value	<na	nd	<na
95% CI of	>na	nd	>na
OR Quart 3	na	nd	na
OR Quart 4	>1.0	nd	>1.0
p Value	<1.0	nd	<1.0
95% CI of	>0.060	nd	>0.060
OR Quart 4	na	nd	na

Insulin-like growth factor 1 receptor

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0484	0.0490	0.0484	0.0644	0.0484	0.0214
Average	0.521	0.0490	0.521	0.0732	0.521	0.0337
Stdev	2.80	0.0562	2.80	0.0681	2.80	0.0410
p (t-test)		0.81		0.75		0.76
Min	9.84E−5	0.00927	9.84E−5	0.000211	9.84E−5	0.000211
Max	21.0	0.0888	21.0	0.164	21.0	0.0795
n (Samp)	229	2	229	4	229	3
n (Patient)	148	2	148	4	148	3
UO only						
Median	nd	nd	0.0520	0.0319	0.0520	0.0108
Average	nd	nd	0.336	0.0570	0.336	0.0108
Stdev	nd	nd	2.14	0.0752	2.14	0.0150
p (t-test)	nd	nd		0.80		0.83
Min	nd	nd	0.000172	0.000211	0.000172	0.000211
Max	nd	nd	21.0	0.164	21.0	0.0214
n (Samp)	nd	nd	196	4	196	2
n (Patient)	nd	nd	124	4	124	2

TABLE 10-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	nd	0.56	nd	0.39	0.33	nd	0.11
SE	0.21	nd	nd	0.15	nd	0.15	0.17	nd	0.15
p	0.83	nd	nd	0.71	nd	0.47	0.32	nd	0.010
nCohort 1	229	nd	nd	229	nd	196	229	nd	196
nCohort 2	2	nd	nd	4	nd	4	3	nd	2
Cutoff 1	0.00767	nd	nd	0.0535	nd	0.00497	0.000208	nd	0.000208
Sens 1	100%	nd	nd	75%	nd	75%	100%	nd	100%
Spec 1	10%	nd	nd	55%	nd	9%	3%	nd	3%
Cutoff 2	0.00767	nd	nd	0.000208	nd	0.000208	0.000208	nd	0.000208
Sens 2	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 2	10%	nd	nd	3%	nd	3%	3%	nd	3%
Cutoff 3	0.00767	nd	nd	0.000208	nd	0.000208	0.000208	nd	0.000208
Sens 3	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 3	10%	nd	nd	3%	nd	3%	3%	nd	3%
Cutoff 4	0.0699	nd	nd	0.0699	nd	0.0769	0.0699	nd	0.0769
Sens 4	50%	nd	nd	50%	nd	25%	33%	nd	0%
Spec 4	70%	nd	nd	70%	nd	70%	70%	nd	70%
Cutoff 5	0.0888	nd	nd	0.0888	nd	0.0888	0.0888	nd	0.0888
Sens 5	0%	nd	nd	25%	nd	25%	0%	nd	0%
Spec 5	81%	nd	nd	81%	nd	81%	81%	nd	81%
Cutoff 6	0.135	nd	nd	0.135	nd	0.135	0.135	nd	0.135
Sens 6	0%	nd	nd	25%	nd	25%	0%	nd	0%
Spec 6	90%	nd	nd	90%	nd	90%	90%	nd	90%
OR Quart 2	0	nd	nd	0	nd	1.0	>1.0	nd	>0
p Value	na	nd	nd	na	nd	1.0	<0.99	nd	<na
95% CI of	na	nd	nd	na	nd	0.061	>0.062	nd	>na
OR Quart 2	na	nd	nd	na	nd	16	na	nd	na
OR Quart 3	0	nd	nd	2.0	nd	0	>0	nd	>0
p Value	na	nd	nd	0.57	nd	na	<na	nd	<na
95% CI of	na	nd	nd	0.18	nd	na	>na	nd	>na
OR Quart 3	na	nd	nd	23	nd	na	na	nd	na
OR Quart 4	1.0	nd	nd	0.98	nd	2.0	>2.1	nd	>2.1
p Value	0.99	nd	nd	0.99	nd	0.57	<0.56	nd	<0.54
95% CI of	0.062	nd	nd	0.060	nd	0.18	>0.18	nd	>0.19
OR Quart 4	17	nd	nd	16	nd	23	na	nd	na

Neural cell adhesion molecule 1

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
sCr or UO	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	181000	111000	181000	166000	181000	162000
Average	186000	154000	186000	177000	186000	163000
Stdev	72800	88700	72800	50000	72800	22700
p (t-test)		0.45		0.76		0.52
Min	190	96200	190	125000	190	140000
Max	520000	256000	520000	245000	520000	187000
n (Samp)	369	3	369	6	369	4
n (Patient)	201	3	201	6	201	4

		48 hr prior to AKI stage	
	sCr only	Cohort 1	Cohort 2
	Median	181000	154000
	Average	186000	154000
	Stdev	72400	19300
	p (t-test)		0.53
	Min	190	140000
	Max	520000	167000
	n (Samp)	376	2
	n (Patient)	205	2

TABLE 10-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

	24 hr prior to AKI stage		48 hr prior to AKI stage	
UO only	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	180000	165000	180000	162000
Average	183000	164000	183000	162000
Stdev	70100	51300	70100	20600
p (t-test)		0.55		0.68
Min	190	111000	190	147000
Max	520000	245000	520000	176000
n (Samp)	339	5	339	2
n (Patient)	178	5	178	2

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.35	nd	nd	0.47	nd	0.40	0.38	0.32	0.39
SE	0.17	nd	nd	0.12	nd	0.14	0.15	0.21	0.21
p	0.39	nd	nd	0.79	nd	0.48	0.43	0.40	0.60
nCohort 1	369	nd	nd	369	nd	339	369	376	339
nCohort 2	3	nd	nd	6	nd	5	4	2	2
Cutoff 1	95600	nd	nd	131000	nd	130000	147000	140000	147000
Sens 1	100%	nd	nd	83%	nd	80%	75%	100%	100%
Spec 1	7%	nd	nd	20%	nd	22%	28%	24%	30%
Cutoff 2	95600	nd	nd	131000	nd	130000	140000	140000	147000
Sens 2	100%	nd	nd	83%	nd	80%	100%	100%	100%
Spec 2	7%	nd	nd	20%	nd	22%	24%	24%	30%
Cutoff 3	95600	nd	nd	125000	nd	109000	140000	140000	147000
Sens 3	100%	nd	nd	100%	nd	100%	100%	100%	100%
Spec 3	7%	nd	nd	16%	nd	12%	24%	24%	30%
Cutoff 4	208000	nd	nd	208000	nd	207000	208000	208000	207000
Sens 4	33%	nd	nd	33%	nd	20%	0%	0%	0%
Spec 4	70%	nd	nd	70%	nd	70%	70%	70%	70%
Cutoff 5	229000	nd	nd	229000	nd	228000	229000	229000	228000
Sens 5	33%	nd	nd	33%	nd	20%	0%	0%	0%
Spec 5	80%	nd	nd	80%	nd	80%	80%	80%	80%
Cutoff 6	268000	nd	nd	268000	nd	262000	268000	266000	262000
Sens 6	0%	nd	nd	0%	nd	0%	0%	0%	0%
Spec 6	90%	nd	nd	90%	nd	90%	90%	90%	90%
OR Quart 2	0	nd	nd	0	nd	0	>1.0	>0	>0
p Value	na	nd	nd	na	nd	na	<0.99	<na	<na
95% CI of	na	nd	nd	na	nd	na	>0.063	>na	>na
OR Quart 2	na	nd	nd	na	nd	na	na	na	na
OR Quart 3	0	nd	nd	1.0	nd	2.0	>2.1	>1.0	>2.1
p Value	na	nd	nd	1.0	nd	0.57	<0.56	<0.99	<0.55
95% CI of	na	nd	nd	0.14	nd	0.18	>0.18	>0.062	>0.18
OR Quart 3	na	nd	nd	7.3	nd	23	na	na	na
OR Quart 4	2.0	nd	nd	1.0	nd	2.0	>1.0	>1.0	>0
p Value	0.57	nd	nd	0.99	nd	0.57	<0.99	<0.99	<na
95% CI of	0.18	nd	nd	0.14	nd	0.18	>0.063	>0.063	>na
OR Quart 4	23	nd	nd	7.3	nd	23	na	na	na

Tumor necrosis factor ligand superfamily member 10

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
sCr or UO						
Median	0.0313	0.0313	0.0313	0.0271	0.0313	0.0313
Average	7.00	1.03	7.00	0.615	7.00	3.95
Stdev	29.0	2.23	29.0	1.44	29.0	7.84
p (t-test)		0.65		0.59		0.83
Min	0.0162	0.0228	0.0162	0.0228	0.0162	0.0162
Max	292	5.02	292	3.56	292	15.7
n (Samp)	290	5	290	6	290	4
n (Patient)	174	5	174	6	174	4
sCr only						
Median	0.0313	0.0271	0.0313	0.0271	nd	nd
Average	6.84	0.0271	6.84	0.0271	nd	nd

TABLE 10-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

Stdev	28.6	0.00598	28.6	0.00598	nd	nd
p (t-test)		0.74		0.74	nd	nd
Min	0.0162	0.0228	0.0162	0.0228	nd	nd
Max	292	0.0313	292	0.0313	nd	nd
n (Samp)	300	2	300	2	nd	nd
n (Patient)	180	2	180	2	nd	nd
UO only						
Median	nd	nd	0.0313	0.0228	0.0313	0.0313
Average	nd	nd	6.81	0.0262	6.81	0.0313
Stdev	nd	nd	29.7	0.00463	29.7	0
p (t-test)	nd	nd		0.61		0.75
Min	nd	nd	0.0162	0.0228	0.0162	0.0313
Max	nd	nd	292	0.0313	292	0.0313
n (Samp)	nd	nd	271	5	271	2
n (Patient)	nd	nd	158	5	158	2

	0 hr prior to AKI stage			24 hr prior to AKI stage			48 hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.48	0.40	nd	0.45	0.40	0.37	0.48	nd	0.46
SE	0.13	0.21	nd	0.12	0.21	0.14	0.15	nd	0.21
p	0.89	0.62	nd	0.67	0.62	0.35	0.89	nd	0.86
nCohort 1	290	300	nd	290	300	271	290	nd	271
nCohort 2	5	2	nd	6	2	5	4	nd	2
Cutoff 1	0.0205	0.0205	nd	0.0205	0.0205	0.0205	0.0269	nd	0.0269
Sens 1	100%	100%	nd	100%	100%	100%	75%	nd	100%
Spec 1	23%	23%	nd	23%	23%	23%	42%	nd	41%
Cutoff 2	0.0205	0.0205	nd	0.0205	0.0205	0.0205	0	nd	0.0269
Sens 2	100%	100%	nd	100%	100%	100%	100%	nd	100%
Spec 2	23%	23%	nd	23%	23%	23%	0%	nd	41%
Cutoff 3	0.0205	0.0205	nd	0.0205	0.0205	0.0205	0	nd	0.0269
Sens 3	100%	100%	nd	100%	100%	100%	100%	nd	100%
Spec 3	23%	23%	nd	23%	23%	23%	0%	nd	41%
Cutoff 4	0.171	0.0943	nd	0.171	0.0943	0.0700	0.171	nd	0.0700
Sens 4	20%	0%	nd	17%	0%	0%	25%	nd	0%
Spec 4	70%	70%	nd	70%	70%	70%	70%	nd	70%
Cutoff 5	3.61	3.61	nd	3.61	3.61	3.32	3.61	nd	3.32
Sens 5	20%	0%	nd	0%	0%	0%	25%	nd	0%
Spec 5	81%	80%	nd	81%	80%	80%	81%	nd	80%
Cutoff 6	14.0	14.0	nd	14.0	14.0	13.4	14.0	nd	13.4
Sens 6	0%	0%	nd	0%	0%	0%	25%	nd	0%
Spec 6	90%	90%	nd	90%	90%	90%	90%	nd	90%
OR Quart 2	0	>0	nd	0	>0	>0	0	nd	>0
p Value	na	<na	nd	na	<na	<na	na	nd	<na
95% CI of	na	>na	nd	na	>na	>na	na	nd	>na
OR Quart 2	na	na	nd	na	na	na	na	nd	na
OR Quart 3	4.2	>2.1	nd	5.3	>2.1	>5.4	2.0	nd	>2.1
p Value	0.21	<0.56	nd	0.13	<0.56	<0.13	0.57	nd	<0.55
95% CI of	0.45	>0.18	nd	0.60	>0.18	>0.61	0.18	nd	>0.19
OR Quart 3	38	na	nd	46	na	na	23	nd	na
OR Quart 4	0	>0	nd	0	>0	>0	1.0	nd	>0
p Value	na	<na	nd	na	<na	<na	0.99	nd	<na
95% CI of	na	>na	nd	na	>na	>na	0.062	nd	>na
OR Quart 4	na	na	nd	na	na	na	17	nd	na

Myeloid differentiation primary response protein MyD88

	24 hr prior to AKI stage	
	Cohort 1	Cohort 2
sCr or UO		
Median	0.000368	0.000368
Average	0.00229	0.000350
Stdev	0.0167	0.000118
p (t-test)		0.84
Min	0.000126	0.000224
Max	0.194	0.000457
n (Samp)	253	3
n (Patient)	144	3

TABLE 10-continued

Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0, R, or I) and in EDTA samples collected from Cohort 2 (subjects who progress to RIFLE stage F) at 0, 24 hours, and 48 hours prior to the subject reaching RIFLE stage I.

UO only		
Median	0.000245	0.000413
Average	0.00239	0.000413
Stdev	0.0171	6.30E−5
p (t-test)		0.87
Min	0.000126	0.000368
Max	0.194	0.000457
n (Samp)	240	2
n (Patient)	129	2

	24 hr prior to AKI stage		
	sCr or UO	sCr only	UO only
AUC	0.53	nd	0.74
SE	0.17	nd	0.20
p	0.87	nd	0.23
nCohort 1	253	nd	240
nCohort 2	3	nd	2
Cutoff 1	0.000126	nd	0.000296
Sens 1	100%	nd	100%
Spec 1	0%	nd	53%
Cutoff 2	0.000126	nd	0.000296
Sens 2	100%	nd	100%
Spec 2	0%	nd	53%
Cutoff 3	0.000126	nd	0.000296
Sens 3	100%	nd	100%
Spec 3	0%	nd	53%
Cutoff 4	0.000368	nd	0.000368
Sens 4	33%	nd	50%
Spec 4	73%	nd	74%
Cutoff 5	0.000457	nd	0.000457
Sens 5	0%	nd	0%
Spec 5	96%	nd	96%
Cutoff 6	0.000457	nd	0.000457
Sens 6	0%	nd	0%
Spec 6	96%	nd	96%
OR Quart 2	1.0	nd	>0
p Value	1.0	nd	<na
95% CI of	0.061	nd	>na
OR Quart 2	16	nd	na
OR Quart 3	0	nd	>2.1
p Value	na	nd	<0.56
95% CI of	na	nd	>0.18
OR Quart 3	na	nd	na
OR Quart 4	1.0	nd	>0
p Value	1.0	nd	<na
95% CI of	0.061	nd	>na
OR Quart 4	16	nd	na

TABLE 11

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

Stromelysin-1:Metalloproteinase inhibitor 2 complex						
	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.487	10.9	0.487	343	0.237	31.8
Average	85.9	135	82.5	295	63.8	151
Stdev	314	197	298	263	303	204
p (t-test)		0.65		0.23		0.44
Min	0.237	0.487	0.237	10.9	0.237	0.487

TABLE 11-continued

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

Max	1930	530	1930	530	1930	530
n (Samp)	49	9	55	3	41	8
n (Patient)	49	9	55	3	41	8

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.79	0.90	0.82
SE	0.094	0.12	0.094
p	0.0019	7.3E−4	6.2E−4
nCohort 1	49	55	41
nCohort 2	9	3	8
Cutoff 1	0.237	3.84	0.237
Sens 1	100%	100%	100%
Spec 1	49%	82%	56%
Cutoff 2	0.237	3.84	0.237
Sens 2	100%	100%	100%
Spec 2	49%	82%	56%
Cutoff 3	0.237	3.84	0.237
Sens 3	100%	100%	100%
Spec 3	49%	82%	56%
Cutoff 4	0.487	0.487	0.487
Sens 4	56%	100%	50%
Spec 4	82%	80%	83%
Cutoff 5	0.487	0.487	0.487
Sens 5	56%	100%	50%
Spec 5	82%	80%	83%
Cutoff 6	201	201	85.2
Sens 6	33%	67%	38%
Spec 6	92%	91%	90%
OR Quart 2	>2.2	>0	>1.1
p Value	<0.55	<na	<0.95
95% CI of	>0.17	>na	>0.061
OR Quart 2	na	na	na
OR Quart 3	>2.3	>0	>4.0
p Value	<0.51	<na	<0.26
95% CI of	>0.19	>na	>0.35
OR Quart 3	na	na	na
OR Quart 4	>7.0	>3.5	>5.3
p Value	<0.097	<0.30	<0.16
95% CI of	>0.71	>0.32	>0.51
OR Quart 4	na	na	na

Heat shock 70 kDa protein 1

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	257	1300	342	1510	225	1090
Average	437	3130	690	3320	449	3360
Stdev	457	4180	1660	3510	484	4460
p (t-test)		5.2E−5		0.015		1.0E−4
Min	0.297	250	0.297	1090	0.297	250
Max	1870	11800	11800	7360	1870	11800
n (Samp)	46	8	51	3	41	7
n (Patient)	46	8	51	3	41	7

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.85	0.93	0.83
SE	0.090	0.10	0.099
p	1.2E−4	4.4E−5	9.2E−4
nCohort 1	46	51	41
nCohort 2	8	3	7
Cutoff 1	755	1020	755
Sens 1	75%	100%	71%
Spec 1	80%	88%	80%
Cutoff 2	408	1020	408
Sens 2	88%	100%	86%
Spec 2	61%	88%	61%

TABLE 11-continued

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

Cutoff 3	225	1020	225
Sens 3	100%	100%	100%
Spec 3	50%	88%	51%
Cutoff 4	634	660	627
Sens 4	75%	100%	71%
Spec 4	72%	71%	71%
Cutoff 5	755	782	755
Sens 5	75%	100%	71%
Spec 5	80%	80%	80%
Cutoff 6	1020	1150	1020
Sens 6	62%	67%	57%
Spec 6	91%	90%	90%
OR Quart 2	>1.0	>0	>1.1
p Value	<1.0	<na	<0.95
95% CI of	>0.056	>na	>0.061
OR Quart 2	na	na	na
OR Quart 3	>2.4	>0	>2.4
p Value	<0.51	<na	<0.50
95% CI of	>0.19	>na	>0.19
OR Quart 3	na	na	na
OR Quart 4	>7.2	>3.5	>6.0
p Value	<0.093	<0.30	<0.14
95% CI of	>0.72	>0.32	>0.56
OR Quart 4	na	na	na

Insulin-like growth factor 1 receptor

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0103	0.0197	0.0103	0.0197	0.0103	0.0292
Average	0.0179	0.0599	0.0245	0.0223	0.0174	0.0664
Stdev	0.0223	0.115	0.0515	0.0152	0.0233	0.122
p (t-test)		0.020		0.94		0.018
Min	0.000123	0.00132	0.000123	0.00862	0.000123	0.00132
Max	0.0976	0.365	0.365	0.0388	0.0976	0.365
n (Samp)	49	9	55	3	41	8
n (Patient)	49	9	55	3	41	8

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.67	0.62	0.72
SE	0.11	0.18	0.11
p	0.11	0.49	0.039
nCohort 1	49	55	41
nCohort 2	9	3	8
Cutoff 1	0.00862	0.00454	0.00862
Sens 1	78%	100%	88%
Spec 1	41%	33%	46%
Cutoff 2	0.00454	0.00454	0.00862
Sens 2	89%	100%	88%
Spec 2	35%	33%	46%
Cutoff 3	0.000519	0.00454	0.000519
Sens 3	100%	100%	100%
Spec 3	24%	33%	29%
Cutoff 4	0.0197	0.0211	0.0169
Sens 4	44%	33%	62%
Spec 4	71%	71%	71%
Cutoff 5	0.0296	0.0339	0.0292
Sens 5	44%	33%	50%
Spec 5	82%	80%	80%
Cutoff 6	0.0423	0.0436	0.0388
Sens 6	22%	0%	38%
Spec 6	92%	91%	90%
OR Quart 2	3.2	>1.0	>1.1
p Value	0.33	<1.0	<0.95
95% CI of	0.30	>0.057	>0.061
OR Quart 2	36	na	na
OR Quart 3	1.0	>1.1	>4.0
p Value	1.0	<0.96	<0.26
95% CI of	0.056	>0.061	>0.35

TABLE 11-continued

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

OR Quart 3	18	na	na
OR Quart 4	4.7	>1.0	>5.3
p Value	0.19	<1.0	<0.16
95% CI of	0.46	>0.057	>0.51
OR Quart 4	49	na	na

72 kDa type IV collagenase:Metalloproteinase inhibitor 2 complex

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	36.4	527	57.4	527	46.9	561
Average	345	4960	853	5570	320	5560
Stdev	585	7200	2700	9040	551	7450
p (t-test)		5.4E−5		0.016		3.4E−5
Min	1.15	1.15	1.15	171	1.15	1.15
Max	2270	16000	16000	16000	2270	16000
n (Samp)	45	9	51	3	40	8
n (Patient)	45	9	51	3	40	8

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.67	0.78	0.68
SE	0.11	0.16	0.11
p	0.10	0.081	0.11
nCohort 1	45	51	40
nCohort 2	9	3	8
Cutoff 1	158	158	234
Sens 1	78%	100%	75%
Spec 1	64%	61%	72%
Cutoff 2	0	158	0
Sens 2	100%	100%	100%
Spec 2	0%	61%	0%
Cutoff 3	0	158	0
Sens 3	100%	100%	100%
Spec 3	0%	61%	0%
Cutoff 4	234	378	189
Sens 4	67%	67%	75%
Spec 4	71%	71%	70%
Cutoff 5	656	660	419
Sens 5	33%	33%	62%
Spec 5	80%	80%	80%
Cutoff 6	1380	1450	1120
Sens 6	33%	33%	38%
Spec 6	91%	90%	90%
OR Quart 2	0	>0	0
p Value	na	<na	na
95% CI of	na	>na	na
OR Quart 2	na	na	na
OR Quart 3	1.6	>2.4	1.0
p Value	0.62	<0.51	1.0
95% CI of	0.23	>0.19	0.12
OR Quart3	12	na	8.6
OR Quart 4	2.2	>1.0	2.5
p Value	0.42	<1.0	0.35
95% CI of	0.33	>0.056	0.36
OR Quart 4	15	na	17

Neural cell adhesion molecule 1

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	2440	3710	2670	4860	2490	3900
Average	3050	5520	3340	7980	3120	5680
Stdev	2340	7260	3480	8950	2140	7560
p (t-test)		5.1E−8		3.7E−7		4.7E−7
Min	6.83	138	6.83	171	173	138

TABLE 11-continued

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

Max	22000	55700	55700	31700	15500	55700
n (Samp)	380	91	448	19	297	79
n (Patient)	380	91	448	19	297	79

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.65	0.68	0.64
SE	0.034	0.069	0.037
p	1.8E−5	0.011	1.2E−4
nCohort 1	380	448	297
nCohort 2	91	19	79
Cutoff 1	2670	2850	2670
Sens 1	70%	74%	71%
Spec 1	54%	55%	53%
Cutoff 2	2130	2200	2080
Sens 2	80%	84%	81%
Spec 2	42%	42%	39%
Cutoff 3	1210	1230	1110
Sens 3	90%	95%	91%
Spec 3	19%	19%	14%
Cutoff 4	3740	3910	3910
Sens 4	49%	53%	49%
Spec 4	70%	70%	70%
Cutoff 5	4550	4730	4750
Sens 5	34%	53%	34%
Spec 5	80%	80%	80%
Cutoff 6	5740	6280	6040
Sens 6	23%	32%	24%
Spec 6	90%	90%	90%
OR Quart 2	1.3	0.66	1.5
p Value	0.57	0.65	0.30
95% CI of	0.57	0.11	0.68
OR Quart2	2.7	4.0	3.5
OR Quart 3	2.5	1.3	2.6
p Value	0.013	0.71	0.017
95% CI of	1.2	0.29	1.2
OR Quart 3	5.1	6.1	5.7
OR Quart 4	3.2	3.5	3.2
p Value	0.0010	0.061	0.0030
95% CI of	1.6	0.94	1.5
OR Quart 4	6.5	13	6.9

Tumor necrosis factor ligand superfamily member 10

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0257	0.0269	0.0257	0.0271	0.0257	0.0285
Average	2.34	4.96	2.69	6.59	2.28	5.68
Stdev	9.11	19.8	11.1	25.2	9.37	21.4
p (t-test)		0.064		0.16		0.040
Min	0.0110	0.0110	0.0110	0.0110	0.0110	0.0139
Max	83.5	134	134	113	83.5	134
n (Samp)	370	89	435	20	291	76
n (Patient)	370	89	435	20	291	76

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.58	0.56	0.58
SE	0.035	0.068	0.038
p	0.015	0.37	0.024
nCohort 1	370	435	291
nCohort 2	89	20	76
Cutoff 1	0.0239	0.0239	0.0239
Sens 1	80%	70%	79%
Spec 1	46%	44%	42%
Cutoff 2	0.0237	0.0239	0.0237
Sens 2	85%	85%	86%
Spec 2	43%	42%	40%

TABLE 11-continued

Comparison of marker levels in enroll urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll urine samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at RIFLE stage I or F were included in Cohort 2.

Cutoff 3	0.0217	0.0217	0.0227
Sens 3	93%	90%	91%
Spec 3	34%	29%	35%
Cutoff 4	0.0439	0.0410	0.0439
Sens 4	21%	30%	22%
Spec 4	74%	70%	75%
Cutoff 5	0.0597	0.0597	0.0526
Sens 5	20%	30%	22%
Spec 5	82%	82%	81%
Cutoff 6	4.27	4.75	3.36
Sens 6	13%	10%	17%
Spec 6	90%	90%	90%
OR Quart 2	7.6	4.2	12
p Value	1.5E−5	0.074	1.1E−5
95% CI of	3.0	0.87	3.9
OR Quart 2	19	20	35
OR Quart 3	6.4	2.0	7.2
p Value	8.4E−5	0.42	4.6E−4
95% CI of	2.5	0.36	2.4
OR Quart 3	16	11	22
OR Quart 4	3.6	3.1	4.9
p Value	0.0094	0.17	0.0057
95% CI of	1.4	0.61	1.6
OR Quart 4	9.3	16	15

TABLE 12

Comparison of marker levels in enroll EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll EDTA samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at stage I or F were included in Cohort 2.

Heat shock 70 kDa protein 1

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	905	1080	nd	nd	949	1080
Average	1300	1080	nd	nd	1200	1080
Stdev	1610	642	nd	nd	1150	642
p (t-test)		0.70	nd	nd		0.77
Min	4.58	261	nd	nd	4.58	261
Max	9150	2280	nd	nd	4430	2280
n (Samp)	46	9	nd	nd	40	9
n (Patient)	46	9	nd	nd	40	9

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.56	nd	0.54
SE	0.11	nd	0.11
p	0.60	nd	0.73
nCohort 1	46	nd	40
nCohort 2	9	nd	9
Cutoff 1	705	nd	618
Sens 1	78%	nd	78%
Spec 1	48%	nd	45%
Cutoff 2	297	nd	297
Sens 2	89%	nd	89%
Spec 2	28%	nd	28%
Cutoff 3	252	nd	252
Sens 3	100%	nd	100%
Spec 3	24%	nd	22%
Cutoff 4	1370	nd	1370
Sens 4	33%	nd	33%
Spec 4	72%	nd	70%
Cutoff 5	1970	nd	1970
Sens 5	11%	nd	11%

TABLE 12-continued

Comparison of marker levels in enroll EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll EDTA samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at stage I or F were included in Cohort 2.

Spec 5	80%	nd	80%
Cutoff 6	3400	nd	3300
Sens 6	0%	nd	0%
Spec 6	91%	nd	90%
OR Quart 2	3.3	nd	3.7
p Value	0.33	nd	0.29
95% CI of	0.29	nd	0.32
OR Quart 2	36	nd	42
OR Quart 3	3.3	nd	3.7
p Value	0.33	nd	0.29
95% CI of	0.29	nd	0.32
OR Quart 3	36	nd	42
OR Quart 4	2.0	nd	2.0
p Value	0.59	nd	0.59
95% CI of	0.16	nd	0.16
OR Quart 4	25	nd	25

Insulin-like growth factor 1 receptor

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0458	0.0656	0.0498	0.0283	0.0514	0.0619
Average	0.465	1.16	0.412	3.91	0.540	0.0941
Stdev	2.58	4.56	2.38	8.68	2.79	0.133
p (t-test)		0.40		0.013		0.54
Min	0.000208	0.000172	0.000172	0.00927	0.000208	0.000172
Max	20.5	19.4	20.5	19.4	20.5	0.543
n (Samp)	68	18	80	5	58	15
n (Patient)	68	18	80	5	58	15

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.57	0.43	0.53
SE	0.078	0.14	0.085
p	0.39	0.62	0.70
nCohort 1	68	80	58
nCohort 2	18	5	15
Cutoff 1	0.0373	0.0134	0.0373
Sens 1	72%	80%	73%
Spec 1	41%	12%	36%
Cutoff 2	0.0134	0.0134	0.0258
Sens 2	83%	80%	80%
Spec 2	12%	12%	26%
Cutoff 3	0.000208	0.00497	0.000208
Sens 3	94%	100%	93%
Spec 3	3%	9%	2%
Cutoff 4	0.0668	0.0766	0.0766
Sens 4	50%	20%	40%
Spec 4	71%	70%	71%
Cutoff 5	0.0839	0.0839	0.0839
Sens 5	33%	20%	33%
Spec 5	84%	80%	83%
Cutoff 6	0.139	0.139	0.167
Sens 6	17%	20%	7%
Spec 6	91%	90%	91%
OR Quart 2	0.94	1.0	1.4
p Value	0.94	0.97	0.67
95% CI of	0.20	0.061	0.27
OR Quart 2	4.4	18	7.5
OR Quart 3	1.0	1.0	1.0
p Value	1.0	0.97	1.0
95% CI of	0.21	0.061	0.17
OR Quart 3	4.7	18	5.8
OR Quart 4	1.6	2.2	1.8
p Value	0.53	0.53	0.48
95% CI of	0.38	0.19	0.36
OR Quart 4	6.7	26	8.9

TABLE 12-continued

Comparison of marker levels in enroll EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll EDTA samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at stage I or F were included in Cohort 2.

Neural cell adhesion molecule 1

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	183000	162000	179000	147000	181000	162000
Average	186000	154000	180000	158000	184000	152000
Stdev	73200	64800	73400	55400	68800	65200
p (t-test)		0.034		0.56		0.036
Min	791	190	190	111000	791	190
Max	494000	331000	494000	230000	461000	331000
n (Samp)	111	28	134	4	100	26
n (Patient)	111	28	134	4	100	26

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.35	0.40	0.35
SE	0.061	0.15	0.064
p	0.018	0.52	0.018
nCohort 1	111	134	100
nCohort 2	28	4	26
Cutoff 1	111000	114000	109000
Sens 1	71%	75%	73%
Spec 1	13%	18%	12%
Cutoff 2	93300	109000	93300
Sens 2	82%	100%	81%
Spec 2	8%	15%	8%
Cutoff 3	79400	109000	79400
Sens 3	93%	100%	92%
Spec 3	5%	15%	5%
Cutoff 4	214000	208000	214000
Sens 4	14%	25%	12%
Spec 4	70%	70%	70%
Cutoff 5	229000	228000	229000
Sens 5	11%	25%	8%
Spec 5	80%	81%	80%
Cutoff 6	268000	265000	265000
Sens 6	4%	0%	4%
Spec 6	90%	90%	90%
OR Quart 2	1.3	0	1.9
p Value	0.72	na	0.43
95% CI of	0.32	na	0.40
OR Quart 2	5.3	na	8.6
OR Quart 3	2.3	1.0	3.2
p Value	0.21	1.0	0.11
95% CI of	0.62	0.060	0.77
OR Quart 3	8.5	17	14
OR Quart 4	3.7	2.1	4.6
p Value	0.042	0.55	0.033
95% CI of	1.0	0.18	1.1
OR Quart 4	13	25	19

Tumor necrosis factor ligand superfamily member 10

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.0247	0.0276	0.0247	0.0313	0.0313	0.0276
Average	10.2	2.74	8.59	7.70	11.1	1.20
Stdev	28.2	9.26	25.9	16.7	29.3	3.76
p (t-test)		0.19		0.93		0.12
Min	0.0162	0.0162	0.0162	0.0162	0.0162	0.0162
Max	172	44.8	172	44.8	172	15.7
n (Samp)	85	26	103	7	78	22
n (Patient)	85	26	103	7	78	22

TABLE 12-continued

Comparison of marker levels in enroll EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R within 48 hrs) and in enroll EDTA samples collected from Cohort 2 (subjects reaching RIFLE stage I or F within 48 hrs). Enroll samples from patients already at stage I or F were included in Cohort 2.

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.47	0.53	0.46
SE	0.065	0.11	0.071
p	0.70	0.82	0.60
nCohort 1	85	103	78
nCohort 2	26	7	22
Cutoff 1	0.0197	0.0197	0.0197
Sens 1	81%	86%	82%
Spec 1	21%	21%	21%
Cutoff 2	0.0197	0.0197	0.0197
Sens 2	81%	86%	82%
Spec 2	21%	21%	21%
Cutoff 3	0	0	0.0162
Sens 3	100%	100%	91%
Spec 3	0%	0%	9%
Cutoff 4	0.0317	0.0317	0.0700
Sens 4	19%	29%	18%
Spec 4	71%	73%	71%
Cutoff 5	2.48	1.46	4.64
Sens 5	12%	29%	9%
Spec 5	80%	81%	81%
Cutoff 6	33.1	25.8	43.5
Sens 6	4%	14%	0%
Spec 6	91%	90%	91%
OR Quart 2	2.8	2.0	2.9
p Value	0.12	0.58	0.17
95% CI of	0.76	0.17	0.64
OR Quart 2	11	23	13
OR Quart 3	2.4	2.1	1.8
p Value	0.20	0.56	0.44
95% CI of	0.63	0.18	0.39
OR Quart 3	9.2	24	8.7
OR Quart 4	1.4	2.0	2.9
p Value	0.67	0.58	0.17
95% CI of	0.32	0.17	0.64
OR Quart 4	5.7	23	13

While the invention has been described and exemplified in sufficient detail for those skilled in this art to make and use it, various alternatives, modifications, and improvements should be apparent without departing from the spirit and scope of the invention. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Modifications therein and other uses will occur to those skilled in the art. These modifications are encompassed within the spirit of the invention and are defined by the scope of the claims.

It will be readily apparent to a person skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

All patents and publications mentioned in the specification are indicative of the levels of those of ordinary skill in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

Other embodiments are set forth within the following claims.

SEQUENCE LISTING

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            20                  25                  30

Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr Glu
        35                  40                  45

Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Leu Asn Pro Gln
    50                  55                  60

Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe Gly Asp
65                  70                  75                  80

Pro Val Val Gln Ser Asp Met Lys His Trp Pro Phe Gln Val Ile Asn
                85                  90                  95

Asp Gly Asp Lys Pro Lys Val Gln Val Ser Tyr Lys Gly Glu Thr Lys
            100                 105                 110

Ala Phe Tyr Pro Glu Glu Ile Ser Ser Met Val Leu Thr Lys Met Lys
        115                 120                 125

Glu Ile Ala Glu Ala Tyr Leu Gly Tyr Pro Val Thr Asn Ala Val Ile
    130                 135                 140

Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr Lys Asp
145                 150                 155                 160

Ala Gly Val Ile Ala Gly Leu Asn Val Leu Arg Ile Ile Asn Glu Pro
                165                 170                 175

Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Arg Thr Gly Lys Gly Glu
            180                 185                 190

Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp Val Ser
        195                 200                 205

Ile Leu Thr Ile Asp Asp Gly Ile Phe Glu Val Lys Ala Thr Ala Gly
    210                 215                 220

Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val Asn His
225                 230                 235                 240

Phe Val Glu Glu Phe Lys Arg Lys His Lys Lys Asp Ile Ser Gln Asn
                245                 250                 255

Lys Arg Ala Val Arg Arg Leu Arg Thr Ala Cys Glu Arg Ala Lys Arg
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Thr Leu Ser Ser Ser Thr Gln Ala Ser Leu Glu Ile Asp Ser Leu Phe
        275                 280                 285

Glu Gly Ile Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe Glu Glu
    290                 295                 300

Leu Cys Ser Asp Leu Phe Arg Ser Thr Leu Glu Pro Val Glu Lys Ala
305                 310                 315                 320

Leu Arg Asp Ala Lys Leu Asp Lys Ala Gln Ile His Asp Leu Val Leu
                325                 330                 335

Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu Gln Asp
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Phe Phe Asn Gly Arg Asp Leu Asn Lys Ser Ile Asn Pro Asp Glu Ala
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Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu Met Gly Asp Lys
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Ser Glu Asn Val Gln Asp Leu Leu Leu Leu Asp Val Ala Pro Leu Ser
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Leu Gly Leu Glu Thr Ala Gly Gly Val Met Thr Ala Leu Ile Lys Arg
                405                 410                 415

Asn Ser Thr Ile Pro Thr Lys Gln Thr Gln Ile Phe Thr Thr Tyr Ser
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Asp Asn Gln Pro Gly Val Leu Ile Gln Val Tyr Glu Gly Glu Arg Ala
        435                 440                 445

Met Thr Lys Asp Asn Asn Leu Leu Gly Arg Phe Glu Leu Ser Gly Ile
    450                 455                 460

Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Ile
465                 470                 475                 480

Asp Ala Asn Gly Ile Leu Asn Val Thr Ala Thr Asp Lys Ser Thr Gly
                485                 490                 495

Lys Ala Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu Ser Lys
            500                 505                 510

Glu Glu Ile Glu Arg Met Val Gln Glu Ala Glu Lys Tyr Lys Ala Glu
        515                 520                 525

Asp Glu Val Gln Arg Glu Arg Val Ser Ala Lys Asn Ala Leu Glu Ser
    530                 535                 540

Tyr Ala Phe Asn Met Lys Ser Ala Val Glu Asp Glu Gly Leu Lys Gly
545                 550                 555                 560

Lys Ile Ser Glu Ala Asp Lys Lys Lys Val Leu Asp Lys Cys Gln Glu
                565                 570                 575

Val Ile Ser Trp Leu Asp Ala Asn Thr Leu Ala Glu Lys Asp Glu Phe
            580                 585                 590

Glu His Lys Arg Lys Glu Leu Glu Gln Val Cys Asn Pro Ile Ile Ser
        595                 600                 605

Gly Leu Tyr Gln Gly Ala Gly Gly Pro Gly Pro Gly Gly Phe Gly Ala
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Gln Gly Pro Lys Gly Gly Ser Gly Ser Gly Pro Thr Ile Glu Glu Val
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Asp
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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

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Leu Val Gln Lys Tyr Leu Glu Asn Tyr Tyr Asp Leu Lys Lys Asp Val
        35                  40                  45

Lys Gln Phe Val Arg Arg Lys Asp Ser Gly Pro Val Val Lys Lys Ile
    50                  55                  60

Arg Glu Met Gln Lys Phe Leu Gly Leu Glu Val Thr Gly Lys Leu Asp
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Ser Asp Thr Leu Glu Val Met Arg Lys Pro Arg Cys Gly Val Pro Asp
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His Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp Leu Pro Lys Asp
        115                 120                 125

Ala Val Asp Ser Ala Val Glu Lys Ala Leu Lys Val Trp Glu Glu Val
    130                 135                 140

Thr Pro Leu Thr Phe Ser Arg Leu Tyr Glu Gly Glu Ala Asp Ile Met
145                 150                 155                 160

Ile Ser Phe Ala Val Arg Glu His Gly Asp Phe Tyr Pro Phe Asp Gly
                165                 170                 175

Pro Gly Asn Val Leu Ala His Ala Tyr Ala Pro Gly Pro Gly Ile Asn
            180                 185                 190

Gly Asp Ala His Phe Asp Asp Asp Glu Gln Trp Thr Lys Asp Thr Thr
        195                 200                 205

Gly Thr Asn Leu Phe Leu Val Ala Ala His Glu Ile Gly His Ser Leu
    210                 215                 220

Gly Leu Phe His Ser Ala Asn Thr Glu Ala Leu Met Tyr Pro Leu Tyr
225                 230                 235                 240

His Ser Leu Thr Asp Leu Thr Arg Phe Arg Leu Ser Gln Asp Asp Ile
                245                 250                 255

Asn Gly Ile Gln Ser Leu Tyr Gly Pro Pro Pro Asp Ser Pro Glu Thr
            260                 265                 270

Pro Leu Val Pro Thr Glu Pro Val Pro Pro Glu Pro Gly Thr Pro Ala
        275                 280                 285

Asn Cys Asp Pro Ala Leu Ser Phe Asp Ala Val Ser Thr Leu Arg Gly
    290                 295                 300

Glu Ile Leu Ile Phe Lys Asp Arg His Phe Trp Arg Lys Ser Leu Arg
305                 310                 315                 320

Lys Leu Glu Pro Glu Leu His Leu Ile Ser Ser Phe Trp Pro Ser Leu
                325                 330                 335

Pro Ser Gly Val Asp Ala Ala Tyr Glu Val Thr Ser Lys Asp Leu Val
            340                 345                 350

Phe Ile Phe Lys Gly Asn Gln Phe Trp Ala Ile Arg Gly Asn Glu Val
        355                 360                 365

Arg Ala Gly Tyr Pro Arg Gly Ile His Thr Leu Gly Phe Pro Pro Thr
    370                 375                 380

Val Arg Lys Ile Asp Ala Ala Ile Ser Asp Lys Glu Lys Asn Lys Thr
385                 390                 395                 400

Tyr Phe Phe Val Glu Asp Lys Tyr Trp Arg Phe Asp Glu Lys Arg Asn
                405                 410                 415

Ser Met Glu Pro Gly Phe Pro Lys Gln Ile Ala Glu Asp Phe Pro Gly
            420                 425                 430

Ile Asp Ser Lys Ile Asp Ala Val Phe Glu Glu Phe Gly Phe Phe Tyr
        435                 440                 445

Phe Phe Thr Gly Ser Ser Gln Leu Glu Phe Asp Pro Asn Ala Lys Lys
    450                 455                 460

Val Thr His Thr Leu Lys Ser Asn Ser Trp Leu Asn Cys
465                 470                 475


<210> SEQ ID NO 3
<211> LENGTH: 660
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 3

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Met Glu Ala Leu Met Ala Arg Gly Ala Leu Thr Gly Pro Leu Arg Ala
1               5                  10                  15

Leu Cys Leu Leu Gly Cys Leu Leu Ser His Ala Ala Ala Ala Pro Ser
            20                  25                  30

Pro Ile Ile Lys Phe Pro Gly Asp Val Ala Pro Lys Thr Asp Lys Glu
        35                  40                  45

Leu Ala Val Gln Tyr Leu Asn Thr Phe Tyr Gly Cys Pro Lys Glu Ser
    50                  55                  60

Cys Asn Leu Phe Val Leu Lys Asp Thr Leu Lys Lys Met Gln Lys Phe
65                  70                  75                  80

Phe Gly Leu Pro Gln Thr Gly Asp Leu Asp Gln Asn Thr Ile Glu Thr
                85                  90                  95

Met Arg Lys Pro Arg Cys Gly Asn Pro Asp Val Ala Asn Tyr Asn Phe
            100                 105                 110

Phe Pro Arg Lys Pro Lys Trp Asp Lys Asn Gln Ile Thr Tyr Arg Ile
        115                 120                 125

Ile Gly Tyr Thr Pro Asp Leu Asp Pro Glu Thr Val Asp Asp Ala Phe
    130                 135                 140

Ala Arg Ala Phe Gln Val Trp Ser Asp Val Thr Pro Leu Arg Phe Ser
145                 150                 155                 160

Arg Ile His Asp Gly Glu Ala Asp Ile Met Ile Asn Phe Gly Arg Trp
                165                 170                 175

Glu His Gly Asp Gly Tyr Pro Phe Asp Gly Lys Asp Gly Leu Leu Ala
            180                 185                 190

His Ala Phe Ala Pro Gly Thr Gly Val Gly Gly Asp Ser His Phe Asp
        195                 200                 205

Asp Asp Glu Leu Trp Thr Leu Gly Glu Gly Gln Val Val Arg Val Lys
    210                 215                 220

Tyr Gly Asn Ala Asp Gly Glu Tyr Cys Lys Phe Pro Phe Leu Phe Asn
225                 230                 235                 240

Gly Lys Glu Tyr Asn Ser Cys Thr Asp Thr Gly Arg Ser Asp Gly Phe
                245                 250                 255

Leu Trp Cys Ser Thr Thr Tyr Asn Phe Glu Lys Asp Gly Lys Tyr Gly
            260                 265                 270

Phe Cys Pro His Glu Ala Leu Phe Thr Met Gly Gly Asn Ala Glu Gly
        275                 280                 285

Gln Pro Cys Lys Phe Pro Phe Arg Phe Gln Gly Thr Ser Tyr Asp Ser
    290                 295                 300

Cys Thr Thr Glu Gly Arg Thr Asp Gly Tyr Arg Trp Cys Gly Thr Thr
305                 310                 315                 320

Glu Asp Tyr Asp Arg Asp Lys Lys Tyr Gly Phe Cys Pro Glu Thr Ala
                325                 330                 335

Met Ser Thr Val Gly Gly Asn Ser Glu Gly Ala Pro Cys Val Phe Pro
            340                 345                 350

Phe Thr Phe Leu Gly Asn Lys Tyr Glu Ser Cys Thr Ser Ala Gly Arg
        355                 360                 365

Ser Asp Gly Lys Met Trp Cys Ala Thr Thr Ala Asn Tyr Asp Asp Asp
    370                 375                 380

Arg Lys Trp Gly Phe Cys Pro Asp Gln Gly Tyr Ser Leu Phe Leu Val
385                 390                 395                 400

Ala Ala His Glu Phe Gly His Ala Met Gly Leu Glu His Ser Gln Asp
                405                 410                 415
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Pro Gly Ala Leu Met Ala Pro Ile Tyr Thr Tyr Thr Lys Asn Phe Arg
            420                 425                 430

Leu Ser Gln Asp Asp Ile Lys Gly Ile Gln Glu Leu Tyr Gly Ala Ser
        435                 440                 445

Pro Asp Ile Asp Leu Gly Thr Gly Pro Thr Pro Thr Leu Gly Pro Val
    450                 455                 460

Thr Pro Glu Ile Cys Lys Gln Asp Ile Val Phe Asp Gly Ile Ala Gln
465                 470                 475                 480

Ile Arg Gly Glu Ile Phe Phe Phe Lys Asp Arg Phe Ile Trp Arg Thr
                485                 490                 495

Val Thr Pro Arg Asp Lys Pro Met Gly Pro Leu Leu Val Ala Thr Phe
            500                 505                 510

Trp Pro Glu Leu Pro Glu Lys Ile Asp Ala Val Tyr Glu Ala Pro Gln
        515                 520                 525

Glu Glu Lys Ala Val Phe Phe Ala Gly Asn Glu Tyr Trp Ile Tyr Ser
    530                 535                 540

Ala Ser Thr Leu Glu Arg Gly Tyr Pro Lys Pro Leu Thr Ser Leu Gly
545                 550                 555                 560

Leu Pro Pro Asp Val Gln Arg Val Asp Ala Ala Phe Asn Trp Ser Lys
                565                 570                 575

Asn Lys Lys Thr Tyr Ile Phe Ala Gly Asp Lys Phe Trp Arg Tyr Asn
            580                 585                 590

Glu Val Lys Lys Lys Met Asp Pro Gly Phe Pro Lys Leu Ile Ala Asp
        595                 600                 605

Ala Trp Asn Ala Ile Pro Asp Asn Leu Asp Ala Val Val Asp Leu Gln
    610                 615                 620

Gly Gly Gly His Ser Tyr Phe Phe Lys Gly Ala Tyr Tyr Leu Lys Leu
625                 630                 635                 640

Glu Asn Gln Ser Leu Lys Ser Val Lys Phe Gly Ser Ile Lys Ser Asp
                645                 650                 655

Trp Leu Gly Cys
            660


<210> SEQ ID NO 4
<211> LENGTH: 220
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

Met Gly Ala Ala Ala Arg Thr Leu Arg Leu Ala Leu Gly Leu Leu Leu
1               5                   10                  15

Leu Ala Thr Leu Leu Arg Pro Ala Asp Ala Cys Ser Cys Ser Pro Val
            20                  25                  30

His Pro Gln Gln Ala Phe Cys Asn Ala Asp Val Val Ile Arg Ala Lys
        35                  40                  45

Ala Val Ser Glu Lys Glu Val Asp Ser Gly Asn Asp Ile Tyr Gly Asn
    50                  55                  60

Pro Ile Lys Arg Ile Gln Tyr Glu Ile Lys Gln Ile Lys Met Phe Lys
65                  70                  75                  80

Gly Pro Glu Lys Asp Ile Glu Phe Ile Tyr Thr Ala Pro Ser Ser Ala
                85                  90                  95

Val Cys Gly Val Ser Leu Asp Val Gly Gly Lys Lys Glu Tyr Leu Ile
            100                 105                 110

Ala Gly Lys Ala Glu Gly Asp Gly Lys Met His Ile Thr Leu Cys Asp
        115                 120                 125
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Phe Ile Val Pro Trp Asp Thr Leu Ser Thr Thr Gln Lys Lys Ser Leu
    130                 135                 140

Asn His Arg Tyr Gln Met Gly Cys Glu Cys Lys Ile Thr Arg Cys Pro
145                 150                 155                 160

Met Ile Pro Cys Tyr Ile Ser Ser Pro Asp Glu Cys Leu Trp Met Asp
                165                 170                 175

Trp Val Thr Glu Lys Asn Ile Asn Gly His Gln Ala Lys Phe Phe Ala
            180                 185                 190

Cys Ile Lys Arg Ser Asp Gly Ser Cys Ala Trp Tyr Arg Gly Ala Ala
        195                 200                 205

Pro Pro Lys Gln Glu Phe Leu Asp Ile Glu Asp Pro
    210                 215                 220


<210> SEQ ID NO 5
<211> LENGTH: 1367
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

Met Lys Ser Gly Ser Gly Gly Gly Ser Pro Thr Ser Leu Trp Gly Leu
1               5                   10                  15

Leu Phe Leu Ser Ala Ala Leu Ser Leu Trp Pro Thr Ser Gly Glu Ile
            20                  25                  30

Cys Gly Pro Gly Ile Asp Ile Arg Asn Asp Tyr Gln Gln Leu Lys Arg
        35                  40                  45

Leu Glu Asn Cys Thr Val Ile Glu Gly Tyr Leu His Ile Leu Leu Ile
    50                  55                  60

Ser Lys Ala Glu Asp Tyr Arg Ser Tyr Arg Phe Pro Lys Leu Thr Val
65                  70                  75                  80

Ile Thr Glu Tyr Leu Leu Leu Phe Arg Val Ala Gly Leu Glu Ser Leu
                85                  90                  95

Gly Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Trp Lys Leu Phe
            100                 105                 110

Tyr Asn Tyr Ala Leu Val Ile Phe Glu Met Thr Asn Leu Lys Asp Ile
        115                 120                 125

Gly Leu Tyr Asn Leu Arg Asn Ile Thr Arg Gly Ala Ile Arg Ile Glu
    130                 135                 140

Lys Asn Ala Asp Leu Cys Tyr Leu Ser Thr Val Asp Trp Ser Leu Ile
145                 150                 155                 160

Leu Asp Ala Val Ser Asn Asn Tyr Ile Val Gly Asn Lys Pro Pro Lys
                165                 170                 175

Glu Cys Gly Asp Leu Cys Pro Gly Thr Met Glu Glu Lys Pro Met Cys
            180                 185                 190

Glu Lys Thr Thr Ile Asn Asn Glu Tyr Asn Tyr Arg Cys Trp Thr Thr
        195                 200                 205

Asn Arg Cys Gln Lys Met Cys Pro Ser Thr Cys Gly Lys Arg Ala Cys
    210                 215                 220

Thr Glu Asn Asn Glu Cys Cys His Pro Glu Cys Leu Gly Ser Cys Ser
225                 230                 235                 240

Ala Pro Asp Asn Asp Thr Ala Cys Val Ala Cys Arg His Tyr Tyr Tyr
                245                 250                 255

Ala Gly Val Cys Val Pro Ala Cys Pro Pro Asn Thr Tyr Arg Phe Glu
            260                 265                 270

Gly Trp Arg Cys Val Asp Arg Asp Phe Cys Ala Asn Ile Leu Ser Ala
        275                 280                 285
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Glu Ser Ser Asp Ser Glu Gly Phe Val Ile His Asp Gly Glu Cys Met
    290                 295                 300

Gln Glu Cys Pro Ser Gly Phe Ile Arg Asn Gly Ser Gln Ser Met Tyr
305                 310                 315                 320

Cys Ile Pro Cys Glu Gly Pro Cys Pro Lys Val Cys Glu Glu Glu Lys
                325                 330                 335

Lys Thr Lys Thr Ile Asp Ser Val Thr Ser Ala Gln Met Leu Gln Gly
            340                 345                 350

Cys Thr Ile Phe Lys Gly Asn Leu Leu Ile Asn Ile Arg Arg Gly Asn
        355                 360                 365

Asn Ile Ala Ser Glu Leu Glu Asn Phe Met Gly Leu Ile Glu Val Val
    370                 375                 380

Thr Gly Tyr Val Lys Ile Arg His Ser His Ala Leu Val Ser Leu Ser
385                 390                 395                 400

Phe Leu Lys Asn Leu Arg Leu Ile Leu Gly Glu Glu Gln Leu Glu Gly
                405                 410                 415

Asn Tyr Ser Phe Tyr Val Leu Asp Asn Gln Asn Leu Gln Gln Leu Trp
            420                 425                 430

Asp Trp Asp His Arg Asn Leu Thr Ile Lys Ala Gly Lys Met Tyr Phe
        435                 440                 445

Ala Phe Asn Pro Lys Leu Cys Val Ser Glu Ile Tyr Arg Met Glu Glu
    450                 455                 460

Val Thr Gly Thr Lys Gly Arg Gln Ser Lys Gly Asp Ile Asn Thr Arg
465                 470                 475                 480

Asn Asn Gly Glu Arg Ala Ser Cys Glu Ser Asp Val Leu His Phe Thr
                485                 490                 495

Ser Thr Thr Thr Ser Lys Asn Arg Ile Ile Ile Thr Trp His Arg Tyr
            500                 505                 510

Arg Pro Pro Asp Tyr Arg Asp Leu Ile Ser Phe Thr Val Tyr Tyr Lys
        515                 520                 525

Glu Ala Pro Phe Lys Asn Val Thr Glu Tyr Asp Gly Gln Asp Ala Cys
    530                 535                 540

Gly Ser Asn Ser Trp Asn Met Val Asp Val Asp Leu Pro Pro Asn Lys
545                 550                 555                 560

Asp Val Glu Pro Gly Ile Leu Leu His Gly Leu Lys Pro Trp Thr Gln
                565                 570                 575

Tyr Ala Val Tyr Val Lys Ala Val Thr Leu Thr Met Val Glu Asn Asp
            580                 585                 590

His Ile Arg Gly Ala Lys Ser Glu Ile Leu Tyr Ile Arg Thr Asn Ala
        595                 600                 605

Ser Val Pro Ser Ile Pro Leu Asp Val Leu Ser Ala Ser Asn Ser Ser
    610                 615                 620

Ser Gln Leu Ile Val Lys Trp Asn Pro Pro Ser Leu Pro Asn Gly Asn
625                 630                 635                 640

Leu Ser Tyr Tyr Ile Val Arg Trp Gln Arg Gln Pro Gln Asp Gly Tyr
                645                 650                 655

Leu Tyr Arg His Asn Tyr Cys Ser Lys Asp Lys Ile Pro Ile Arg Lys
            660                 665                 670

Tyr Ala Asp Gly Thr Ile Asp Ile Glu Glu Val Thr Glu Asn Pro Lys
        675                 680                 685

Thr Glu Val Cys Gly Gly Glu Lys Gly Pro Cys Cys Ala Cys Pro Lys
    690                 695                 700
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Thr Glu Ala Glu Lys Gln Ala Glu Lys Glu Glu Ala Glu Tyr Arg Lys
705                 710                 715                 720

Val Phe Glu Asn Phe Leu His Asn Ser Ile Phe Val Pro Arg Pro Glu
                725                 730                 735

Arg Lys Arg Arg Asp Val Met Gln Val Ala Asn Thr Thr Met Ser Ser
            740                 745                 750

Arg Ser Arg Asn Thr Thr Ala Ala Asp Thr Tyr Asn Ile Thr Asp Pro
        755                 760                 765

Glu Glu Leu Glu Thr Glu Tyr Pro Phe Phe Glu Ser Arg Val Asp Asn
    770                 775                 780

Lys Glu Arg Thr Val Ile Ser Asn Leu Arg Pro Phe Thr Leu Tyr Arg
785                 790                 795                 800

Ile Asp Ile His Ser Cys Asn His Glu Ala Glu Lys Leu Gly Cys Ser
                805                 810                 815

Ala Ser Asn Phe Val Phe Ala Arg Thr Met Pro Ala Glu Gly Ala Asp
            820                 825                 830

Asp Ile Pro Gly Pro Val Thr Trp Glu Pro Arg Pro Glu Asn Ser Ile
        835                 840                 845

Phe Leu Lys Trp Pro Glu Pro Glu Asn Pro Asn Gly Leu Ile Leu Met
    850                 855                 860

Tyr Glu Ile Lys Tyr Gly Ser Gln Val Glu Asp Gln Arg Glu Cys Val
865                 870                 875                 880

Ser Arg Gln Glu Tyr Arg Lys Tyr Gly Gly Ala Lys Leu Asn Arg Leu
                885                 890                 895

Asn Pro Gly Asn Tyr Thr Ala Arg Ile Gln Ala Thr Ser Leu Ser Gly
            900                 905                 910

Asn Gly Ser Trp Thr Asp Pro Val Phe Phe Tyr Val Gln Ala Lys Thr
        915                 920                 925

Gly Tyr Glu Asn Phe Ile His Leu Ile Ile Ala Leu Pro Val Ala Val
    930                 935                 940

Leu Leu Ile Val Gly Gly Leu Val Ile Met Leu Tyr Val Phe His Arg
945                 950                 955                 960

Lys Arg Asn Asn Ser Arg Leu Gly Asn Gly Val Leu Tyr Ala Ser Val
                965                 970                 975

Asn Pro Glu Tyr Phe Ser Ala Ala Asp Val Tyr Val Pro Asp Glu Trp
            980                 985                 990

Glu Val Ala Arg Glu Lys Ile Thr  Met Ser Arg Glu Leu  Gly Gln Gly
        995                 1000                1005

Ser Phe  Gly Met Val Tyr Glu  Gly Val Ala Lys Gly  Val Val Lys
    1010                1015                1020

Asp Glu  Pro Glu Thr Arg Val  Ala Ile Lys Thr Val  Asn Glu Ala
    1025                1030                1035

Ala Ser  Met Arg Glu Arg Ile  Glu Phe Leu Asn Glu  Ala Ser Val
    1040                1045                1050

Met Lys  Glu Phe Asn Cys His  His Val Val Arg Leu  Leu Gly Val
    1055                1060                1065

Val Ser  Gln Gly Gln Pro Thr  Leu Val Ile Met Glu  Leu Met Thr
    1070                1075                1080

Arg Gly  Asp Leu Lys Ser Tyr  Leu Arg Ser Leu Arg  Pro Glu Met
    1085                1090                1095

Glu Asn  Asn Pro Val Leu Ala  Pro Pro Ser Leu Ser  Lys Met Ile
    1100                1105                1110
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Gln Met  Ala Gly Glu Ile Ala  Asp Gly Met Ala Tyr  Leu Asn Ala
    1115                1120                1125

Asn Lys  Phe Val His Arg Asp  Leu Ala Ala Arg Asn  Cys Met Val
    1130                1135                1140

Ala Glu  Asp Phe Thr Val Lys  Ile Gly Asp Phe Gly  Met Thr Arg
    1145                1150                1155

Asp Ile  Tyr Glu Thr Asp Tyr  Tyr Arg Lys Gly Gly  Lys Gly Leu
    1160                1165                1170

Leu Pro  Val Arg Trp Met Ser  Pro Glu Ser Leu Lys  Asp Gly Val
    1175                1180                1185

Phe Thr  Thr Tyr Ser Asp Val  Trp Ser Phe Gly Val  Val Leu Trp
    1190                1195                1200

Glu Ile  Ala Thr Leu Ala Glu  Gln Pro Tyr Gln Gly  Leu Ser Asn
    1205                1210                1215

Glu Gln  Val Leu Arg Phe Val  Met Glu Gly Gly Leu  Leu Asp Lys
    1220                1225                1230

Pro Asp  Asn Cys Pro Asp Met  Leu Phe Glu Leu Met  Arg Met Cys
    1235                1240                1245

Trp Gln  Tyr Asn Pro Lys Met  Arg Pro Ser Phe Leu  Glu Ile Ile
    1250                1255                1260

Ser Ser  Ile Lys Glu Glu Met  Glu Pro Gly Phe Arg  Glu Val Ser
    1265                1270                1275

Phe Tyr  Tyr Ser Glu Glu Asn  Lys Leu Pro Glu Pro  Glu Glu Leu
    1280                1285                1290

Asp Leu  Glu Pro Glu Asn Met  Glu Ser Val Pro Leu  Asp Pro Ser
    1295                1300                1305

Ala Ser  Ser Ser Ser Leu Pro  Leu Pro Asp Arg His  Ser Gly His
    1310                1315                1320

Lys Ala  Glu Asn Gly Pro Gly  Pro Gly Val Leu Val  Leu Arg Ala
    1325                1330                1335

Ser Phe  Asp Glu Arg Gln Pro  Tyr Ala His Met Asn  Gly Gly Arg
    1340                1345                1350

Lys Asn  Glu Arg Ala Leu Pro  Leu Pro Gln Ser Ser  Thr Cys
    1355                1360                1365


<210> SEQ ID NO 6
<211> LENGTH: 296
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

Met Ala Ala Gly Gly Pro Gly Ala Gly Ser Ala Ala Pro Val Ser Ser
1               5                   10                  15

Thr Ser Ser Leu Pro Leu Ala Ala Leu Asn Met Arg Val Arg Arg Arg
            20                  25                  30

Leu Ser Leu Phe Leu Asn Val Arg Thr Gln Val Ala Ala Asp Trp Thr
        35                  40                  45

Ala Leu Ala Glu Glu Met Asp Phe Glu Tyr Leu Glu Ile Arg Gln Leu
    50                  55                  60

Glu Thr Gln Ala Asp Pro Thr Gly Arg Leu Leu Asp Ala Trp Gln Gly
65                  70                  75                  80

Arg Pro Gly Ala Ser Val Gly Arg Leu Leu Glu Leu Leu Thr Lys Leu
                85                  90                  95

Gly Arg Asp Asp Val Leu Leu Glu Leu Gly Pro Ser Ile Glu Glu Asp
            100                 105                 110
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```
Cys Gln Lys Tyr Ile Leu Lys Gln Gln Glu Glu Ala Glu Lys Pro
        115                 120                 125

Leu Gln Val Ala Ala Val Asp Ser Ser Val Pro Arg Thr Ala Glu Leu
    130                 135                 140

Ala Gly Ile Thr Thr Leu Asp Asp Pro Leu Gly His Met Pro Glu Arg
145                 150                 155                 160

Phe Asp Ala Phe Ile Cys Tyr Cys Pro Ser Asp Ile Gln Phe Val Gln
                165                 170                 175

Glu Met Ile Arg Gln Leu Glu Gln Thr Asn Tyr Arg Leu Lys Leu Cys
            180                 185                 190

Val Ser Asp Arg Asp Val Leu Pro Gly Thr Cys Val Trp Ser Ile Ala
        195                 200                 205

Ser Glu Leu Ile Glu Lys Arg Cys Arg Arg Met Val Val Val Val Ser
    210                 215                 220

Asp Asp Tyr Leu Gln Ser Lys Glu Cys Asp Phe Gln Thr Lys Phe Ala
225                 230                 235                 240

Leu Ser Leu Ser Pro Gly Ala His Gln Lys Arg Leu Ile Pro Ile Lys
                245                 250                 255

Tyr Lys Ala Met Lys Lys Glu Phe Pro Ser Ile Leu Arg Phe Ile Thr
            260                 265                 270

Val Cys Asp Tyr Thr Asn Pro Cys Thr Lys Ser Trp Phe Trp Thr Arg
        275                 280                 285

Leu Ala Lys Ala Leu Ser Leu Pro
    290                 295


<210> SEQ ID NO 7
<211> LENGTH: 1304
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 7

Met Gln Leu Lys Ile Met Pro Lys Lys Lys Arg Leu Ser Ala Gly Arg
1               5                   10                  15

Val Pro Leu Ile Leu Phe Leu Cys Gln Met Ile Ser Ala Leu Glu Val
            20                  25                  30

Pro Leu Asp Pro Lys Leu Leu Glu Asp Leu Val Gln Pro Pro Thr Ile
        35                  40                  45

Thr Gln Gln Ser Pro Lys Asp Tyr Ile Ile Asp Pro Arg Glu Asn Ile
    50                  55                  60

Val Ile Gln Cys Glu Ala Lys Gly Lys Pro Pro Pro Ser Phe Ser Trp
65                  70                  75                  80

Thr Arg Asn Gly Thr His Phe Asp Ile Asp Lys Asp Pro Leu Val Thr
                85                  90                  95

Met Lys Pro Gly Thr Gly Thr Leu Ile Ile Asn Ile Met Ser Glu Gly
            100                 105                 110

Lys Ala Glu Thr Tyr Glu Gly Val Tyr Gln Cys Thr Ala Arg Asn Glu
        115                 120                 125

Arg Gly Ala Ala Val Ser Asn Asn Ile Val Val Arg Pro Ser Arg Ser
    130                 135                 140

Pro Leu Trp Thr Lys Glu Lys Leu Glu Pro Ile Thr Leu Gln Ser Gly
145                 150                 155                 160

Gln Ser Leu Val Leu Pro Cys Arg Pro Pro Ile Gly Leu Pro Pro Pro
                165                 170                 175

Ile Ile Phe Trp Met Asp Asn Ser Phe Gln Arg Leu Pro Gln Ser Glu
            180                 185                 190
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```
Arg Val Ser Gln Gly Leu Asn Gly Asp Leu Tyr Phe Ser Asn Val Leu
        195                 200                 205

Pro Glu Asp Thr Arg Glu Asp Tyr Ile Cys Tyr Ala Arg Phe Asn His
    210                 215                 220

Thr Gln Thr Ile Gln Gln Lys Gln Pro Ile Ser Val Lys Val Ile Ser
225                 230                 235                 240

Val Asp Glu Leu Asn Asp Thr Ile Ala Ala Asn Leu Ser Asp Thr Glu
                245                 250                 255

Phe Tyr Gly Ala Lys Ser Ser Arg Glu Arg Pro Pro Thr Phe Leu Thr
            260                 265                 270

Pro Glu Gly Asn Ala Ser Asn Lys Glu Glu Leu Arg Gly Asn Val Leu
        275                 280                 285

Ser Leu Glu Cys Ile Ala Glu Gly Leu Pro Thr Pro Ile Ile Tyr Trp
    290                 295                 300

Ala Lys Glu Asp Gly Met Leu Pro Lys Asn Arg Thr Val Tyr Lys Asn
305                 310                 315                 320

Phe Glu Lys Thr Leu Gln Ile Ile His Val Ser Glu Ala Asp Ser Gly
                325                 330                 335

Asn Tyr Gln Cys Ile Ala Lys Asn Ala Leu Gly Ala Ile His His Thr
            340                 345                 350

Ile Ser Val Arg Val Lys Ala Ala Pro Tyr Trp Ile Thr Ala Pro Gln
        355                 360                 365

Asn Leu Val Leu Ser Pro Gly Glu Asp Gly Thr Leu Ile Cys Arg Ala
    370                 375                 380

Asn Gly Asn Pro Lys Pro Arg Ile Ser Trp Leu Thr Asn Gly Val Pro
385                 390                 395                 400

Ile Glu Ile Ala Pro Asp Asp Pro Ser Arg Lys Ile Asp Gly Asp Thr
                405                 410                 415

Ile Ile Phe Ser Asn Val Gln Glu Arg Ser Ser Ala Val Tyr Gln Cys
            420                 425                 430

Asn Ala Ser Asn Glu Tyr Gly Tyr Leu Leu Ala Asn Ala Phe Val Asn
        435                 440                 445

Val Leu Ala Glu Pro Pro Arg Ile Leu Thr Pro Ala Asn Thr Leu Tyr
    450                 455                 460

Gln Val Ile Ala Asn Arg Pro Ala Leu Leu Asp Cys Ala Phe Phe Gly
465                 470                 475                 480

Ser Pro Leu Pro Thr Ile Glu Trp Phe Lys Gly Ala Lys Gly Ser Ala
                485                 490                 495

Leu His Glu Asp Ile Tyr Val Leu His Glu Asn Gly Thr Leu Glu Ile
            500                 505                 510

Pro Val Ala Gln Lys Asp Ser Thr Gly Thr Tyr Thr Cys Val Ala Arg
        515                 520                 525

Asn Lys Leu Gly Met Ala Lys Asn Glu Val His Leu Glu Ile Lys Asp
    530                 535                 540

Pro Thr Trp Ile Val Lys Gln Pro Glu Tyr Ala Val Val Gln Arg Gly
545                 550                 555                 560

Ser Met Val Ser Phe Glu Cys Lys Val Lys His Asp His Thr Leu Ser
                565                 570                 575

Leu Thr Val Leu Trp Leu Lys Asp Asn Arg Glu Leu Pro Ser Asp Glu
            580                 585                 590

Arg Phe Thr Val Asp Lys Asp His Leu Val Val Ala Asp Val Ser Asp
        595                 600                 605
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```
Asp Asp Ser Gly Thr Tyr Thr Cys Val Ala Asn Thr Thr Leu Asp Ser
    610                 615                 620

Val Ser Ala Ser Ala Val Leu Ser Val Val Ala Pro Thr Pro Thr Pro
625                 630                 635                 640

Ala Pro Val Tyr Asp Val Pro Asn Pro Pro Phe Asp Leu Glu Leu Thr
                645                 650                 655

Asp Gln Leu Asp Lys Ser Val Gln Leu Ser Trp Thr Pro Gly Asp Asp
            660                 665                 670

Asn Asn Ser Pro Ile Thr Lys Phe Ile Ile Glu Tyr Glu Asp Ala Met
        675                 680                 685

His Lys Pro Gly Leu Trp His His Gln Thr Glu Val Ser Gly Thr Gln
    690                 695                 700

Thr Thr Ala Gln Leu Lys Leu Ser Pro Tyr Val Asn Tyr Ser Phe Arg
705                 710                 715                 720

Val Met Ala Val Asn Ser Ile Gly Lys Ser Leu Pro Ser Glu Ala Ser
                725                 730                 735

Glu Gln Tyr Leu Thr Lys Ala Ser Glu Pro Asp Lys Asn Pro Thr Ala
            740                 745                 750

Val Glu Gly Leu Gly Ser Glu Pro Asp Asn Leu Val Ile Thr Trp Lys
        755                 760                 765

Pro Leu Asn Gly Phe Glu Ser Asn Gly Pro Gly Leu Gln Tyr Lys Val
    770                 775                 780

Ser Trp Arg Gln Lys Asp Gly Asp Asp Glu Trp Thr Ser Val Val Val
785                 790                 795                 800

Ala Asn Val Ser Lys Tyr Ile Val Ser Gly Thr Pro Thr Phe Val Pro
                805                 810                 815

Tyr Leu Ile Lys Val Gln Ala Leu Asn Asp Met Gly Phe Ala Pro Glu
            820                 825                 830

Pro Ala Val Val Met Gly His Ser Gly Glu Asp Leu Pro Met Val Ala
        835                 840                 845

Pro Gly Asn Val Arg Val Asn Val Val Asn Ser Thr Leu Ala Glu Val
    850                 855                 860

His Trp Asp Pro Val Pro Leu Lys Ser Ile Arg Gly His Leu Gln Gly
865                 870                 875                 880

Tyr Arg Ile Tyr Tyr Trp Lys Thr Gln Ser Ser Ser Lys Arg Asn Arg
                885                 890                 895

Arg His Ile Glu Lys Lys Ile Leu Thr Phe Gln Gly Ser Lys Thr His
            900                 905                 910

Gly Met Leu Pro Gly Leu Glu Pro Phe Ser His Tyr Thr Leu Asn Val
        915                 920                 925

Arg Val Val Asn Gly Lys Gly Glu Gly Pro Ala Ser Pro Asp Arg Val
    930                 935                 940

Phe Asn Thr Pro Glu Gly Val Pro Ser Ala Pro Ser Ser Leu Lys Ile
945                 950                 955                 960

Val Asn Pro Thr Leu Asp Ser Leu Thr Leu Glu Trp Asp Pro Pro Ser
                965                 970                 975

His Pro Asn Gly Ile Leu Thr Glu Tyr Thr Leu Lys Tyr Gln Pro Ile
            980                 985                 990

Asn Ser Thr His Glu Leu Gly Pro  Leu Val Asp Leu Lys  Ile Pro Ala
        995                 1000                1005

Asn Lys  Thr Arg Trp Thr Leu  Lys Asn Leu Asn Phe  Ser Thr Arg
    1010                1015                1020
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Tyr Lys  Phe Tyr Phe Tyr Ala  Gln Thr Ser Ala Gly  Ser Gly Ser
    1025                1030                1035

Gln Ile  Thr Glu Glu Ala Val  Thr Thr Val Asp Glu  Ala Gly Ile
    1040                1045                1050

Leu Pro  Pro Asp Val Gly Ala  Gly Lys Val Gln Ala  Val Asn Thr
    1055                1060                1065

Arg Ile  Ser Asn Leu Thr Ala  Ala Ala Ala Glu Thr  Tyr Ala Asn
    1070                1075                1080

Ile Ser  Trp Glu Tyr Glu Gly  Pro Glu His Val Asn  Phe Tyr Val
    1085                1090                1095

Glu Tyr  Gly Val Ala Gly Ser  Lys Glu Glu Trp Arg  Lys Glu Ile
    1100                1105                1110

Val Asn  Gly Ser Arg Ser Phe  Phe Gly Leu Lys Gly  Leu Met Pro
    1115                1120                1125

Gly Thr  Ala Tyr Lys Val Arg  Val Gly Ala Val Gly  Asp Ser Gly
    1130                1135                1140

Phe Val  Ser Ser Glu Asp Val  Phe Glu Thr Gly Pro  Ala Met Ala
    1145                1150                1155

Ser Arg  Gln Val Asp Ile Ala  Thr Gln Gly Trp Phe  Ile Gly Leu
    1160                1165                1170

Met Cys  Ala Val Ala Leu Leu  Ile Leu Ile Leu Leu  Ile Val Cys
    1175                1180                1185

Phe Ile  Arg Arg Asn Lys Gly  Gly Lys Tyr Pro Val  Lys Glu Lys
    1190                1195                1200

Glu Asp  Ala His Ala Asp Pro  Glu Ile Gln Pro Met  Lys Glu Asp
    1205                1210                1215

Asp Gly  Thr Phe Gly Glu Tyr  Ser Asp Ala Glu Asp  His Lys Pro
    1220                1225                1230

Leu Lys  Lys Gly Ser Arg Thr  Pro Ser Asp Arg Thr  Val Lys Lys
    1235                1240                1245

Glu Asp  Ser Asp Asp Ser Leu  Val Asp Tyr Gly Glu  Gly Val Asn
    1250                1255                1260

Gly Gln  Phe Asn Glu Asp Gly  Ser Phe Ile Gly Gln  Tyr Ser Gly
    1265                1270                1275

Lys Lys  Glu Lys Glu Pro Ala  Glu Gly Asn Glu Ser  Ser Glu Ala
    1280                1285                1290

Pro Ser  Pro Val Asn Ala Met  Asn Ser Phe Val
    1295                1300


<210> SEQ ID NO 8
<211> LENGTH: 281
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

Met Ala Met Met Glu Val Gln Gly Gly Pro Ser Leu Gly Gln Thr Cys
1               5                  10                  15

Val Leu Ile Val Ile Phe Thr Val Leu Leu Gln Ser Leu Cys Val Ala
            20                  25                  30

Val Thr Tyr Val Tyr Phe Thr Asn Glu Leu Lys Gln Met Gln Asp Lys
        35                  40                  45

Tyr Ser Lys Ser Gly Ile Ala Cys Phe Leu Lys Glu Asp Asp Ser Tyr
    50                  55                  60

Trp Asp Pro Asn Asp Glu Glu Ser Met Asn Ser Pro Cys Trp Gln Val
65                  70                  75                  80
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Lys Trp Gln Leu Arg Gln Leu Val Arg Lys Met Ile Leu Arg Thr Ser
                85                  90                  95

Glu Glu Thr Ile Ser Thr Val Gln Glu Lys Gln Gln Asn Ile Ser Pro
            100                 105                 110

Leu Val Arg Glu Arg Gly Pro Gln Arg Val Ala Ala His Ile Thr Gly
        115                 120                 125

Thr Arg Gly Arg Ser Asn Thr Leu Ser Ser Pro Asn Ser Lys Asn Glu
    130                 135                 140

Lys Ala Leu Gly Arg Lys Ile Asn Ser Trp Glu Ser Ser Arg Ser Gly
145                 150                 155                 160

His Ser Phe Leu Ser Asn Leu His Leu Arg Asn Gly Glu Leu Val Ile
                165                 170                 175

His Glu Lys Gly Phe Tyr Tyr Ile Tyr Ser Gln Thr Tyr Phe Arg Phe
            180                 185                 190

Gln Glu Glu Ile Lys Glu Asn Thr Lys Asn Asp Lys Gln Met Val Gln
        195                 200                 205

Tyr Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp Pro Ile Leu Leu Met Lys
    210                 215                 220

Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr
225                 230                 235                 240

Ser Ile Tyr Gln Gly Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile
                245                 250                 255

Phe Val Ser Val Thr Asn Glu His Leu Ile Asp Met Asp His Glu Ala
            260                 265                 270

Ser Phe Phe Gly Ala Phe Leu Val Gly
        275                 280


<210> SEQ ID NO 9
<211> LENGTH: 418
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys
1               5                   10                  15

Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala
            20                  25                  30

Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
        35                  40                  45

Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln
    50                  55                  60

Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser
65                  70                  75                  80

Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr
                85                  90                  95

His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro
            100                 105                 110

Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn
        115                 120                 125

Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu
    130                 135                 140

Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys
145                 150                 155                 160

Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu
                165                 170                 175
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Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys
            180                 185                 190

Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu
        195                 200                 205

Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
    210                 215                 220

Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val
225                 230                 235                 240

Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
                245                 250                 255

Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
            260                 265                 270

Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
        275                 280                 285

Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
    290                 295                 300

Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
305                 310                 315                 320

Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
                325                 330                 335

Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
            340                 345                 350

Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
        355                 360                 365

Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
    370                 375                 380

Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
385                 390                 395                 400

Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
                405                 410                 415

Gln Lys


<210> SEQ ID NO 10
<211> LENGTH: 267
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 10

Met Thr Leu Gly Arg Arg Leu Ala Cys Leu Phe Leu Ala Cys Val Leu
1               5                   10                  15

Pro Ala Leu Leu Leu Gly Gly Thr Ala Leu Ala Ser Glu Ile Val Gly
            20                  25                  30

Gly Arg Arg Ala Arg Pro His Ala Trp Pro Phe Met Val Ser Leu Gln
        35                  40                  45

Leu Arg Gly Gly His Phe Cys Gly Ala Thr Leu Ile Ala Pro Asn Phe
    50                  55                  60

Val Met Ser Ala Ala His Cys Val Ala Asn Val Asn Val Arg Ala Val
65                  70                  75                  80

Arg Val Val Leu Gly Ala His Asn Leu Ser Arg Arg Glu Pro Thr Arg
                85                  90                  95

Gln Val Phe Ala Val Gln Arg Ile Phe Glu Asn Gly Tyr Asp Pro Val
            100                 105                 110

Asn Leu Leu Asn Asp Ile Val Ile Leu Gln Leu Asn Gly Ser Ala Thr
        115                 120                 125
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Ile Asn Ala Asn Val Gln Val Ala Gln Leu Pro Ala Gln Gly Arg Arg
    130                 135                 140

Leu Gly Asn Gly Val Gln Cys Leu Ala Met Gly Trp Gly Leu Leu Gly
145                 150                 155                 160

Arg Asn Arg Gly Ile Ala Ser Val Leu Gln Glu Leu Asn Val Thr Val
                165                 170                 175

Val Thr Ser Leu Cys Arg Arg Ser Asn Val Cys Thr Leu Val Arg Gly
            180                 185                 190

Arg Gln Ala Gly Val Cys Phe Gly Asp Ser Gly Ser Pro Leu Val Cys
        195                 200                 205

Asn Gly Leu Ile His Gly Ile Ala Ser Phe Val Arg Gly Gly Cys Ala
    210                 215                 220

Ser Gly Leu Tyr Pro Asp Ala Phe Ala Pro Val Ala Gln Phe Val Asn
225                 230                 235                 240

Trp Ile Asp Ser Ile Ile Gln Arg Ser Glu Asp Asn Pro Cys Pro His
                245                 250                 255

Pro Arg Asp Pro Asp Pro Ala Ser Arg Thr His
            260                 265
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We claim:

1. A method for evaluating renal status in a subject, comprising:

performing one or more assays configured to detect Stromelysin-1:Metalloproteinase inhibitor 2 complex, on a body fluid sample obtained from the subject to provide an assay result;

correlating the assay result(s) to the renal status of the subject by introducing the body fluid sample obtained from the subject into an assay instrument which contacts all or a portion of the body fluid sample with a binding reagent which specifically binds for detection Stromelysin-1:Metalloproteinase inhibitor 2 complex, and (ii) generates an assay result indicative of binding of Stromelysin-1:Metalloproteinase inhibitor 2 complex to the binding reagent; and

correlating the assay result generated by the assay instrument to the renal status of the subject by using the assay result to assign the subject to a predetermined subpopulation of individuals having a known predisposition of a future acute renal injury within 72 hours of the time at which the body fluid sample is obtained; and

treating the patient based on the predetermined subpopulation of individuals to which the patient is assigned, wherein the treatment comprises one or more of initiating renal replacement therapy, withdrawing delivery of compounds that are known to be damaging to the kidney, delaying or avoiding procedures that are known to be damaging to the kidney, and modifying diuretic administration.

2. A method according to claim **1**, wherein said assay result comprises a measured concentration of Stromelysin-1:Metalloproteinase inhibitor 2 complex.

3. A method according to claim **1**, wherein a plurality of assay results are combined using a function that converts the plurality of assay results into a single composite result.

4. A method according to claim **1**, wherein the subject is selected for evaluation of renal status based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF.

5. A method according to claim **1**, wherein the subject is selected for evaluation of renal status based on an existing diagnosis of one or more of congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, sepsis, injury to renal function, reduced renal function, or ARF, or based on undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery, or based on exposure to NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin.

6. A method according to claim **1**, wherein said one or more future changes in renal status comprise one or more of a future injury to renal function, future reduced renal function, future improvement in renal function, and future acute renal failure (ARF) within 48 hours of the time at which the body fluid sample is obtained.

7. A method according to claim **1**, wherein said one or more future changes in renal status comprise one or more of a future injury to renal function, future reduced renal function, future improvement in renal function, and future acute renal failure (ARF) within 24 hours of the time at which the body fluid sample is obtained.

8. A method according to claim **1**, wherein the subject is in RIFLE stage 0 or R.

9. A method according to claim **8**, wherein the subject is in RIFLE stage 0 or R, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 72 hours.

10. A method according to claim **1**, wherein the subject is not in acute renal failure.

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